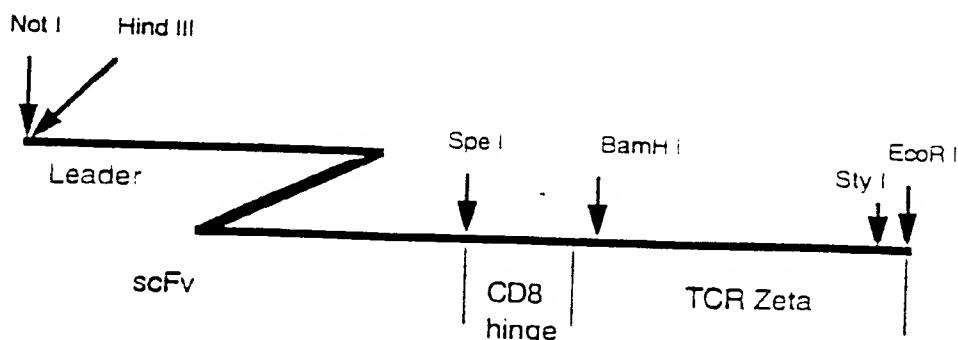


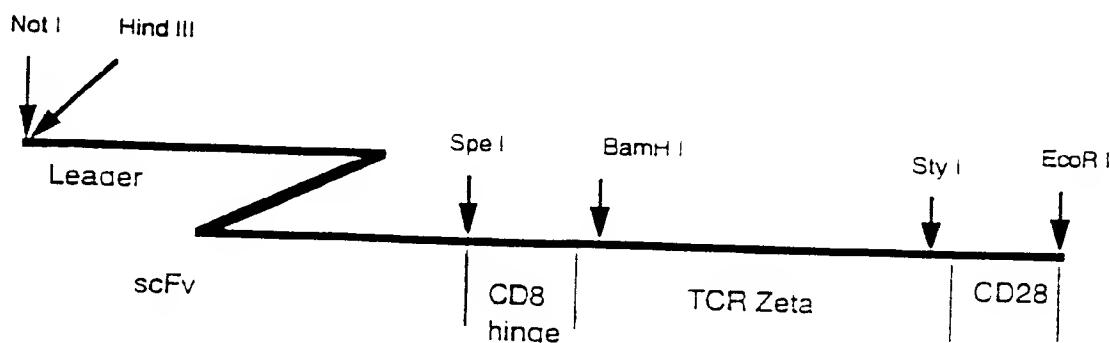
1/40

FIG. 1  
Construct cassettes cloned into pBluescript SK +

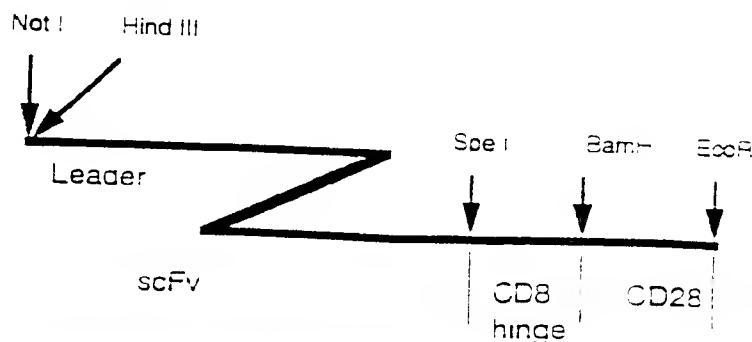
scFv / CD8 / Zeta Chimeric Receptor



scFv / CD8 / Zeta-CD28 fusion Chimeric Receptor



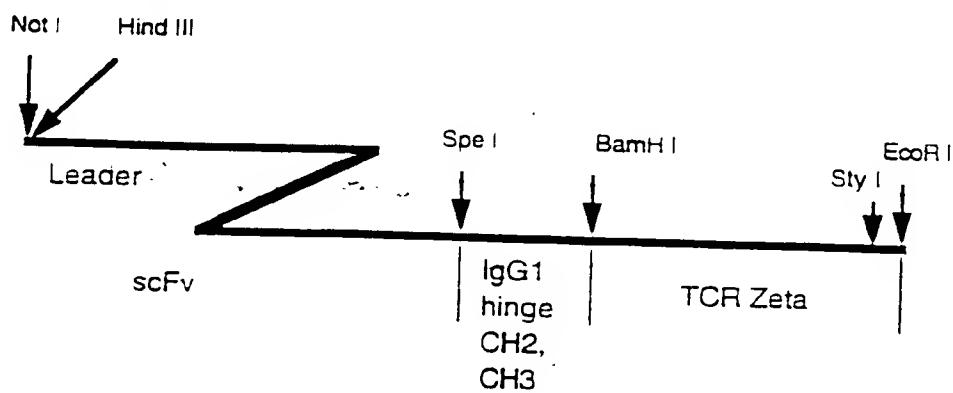
scFv / CD8 / CD28 Chimeric Receptor



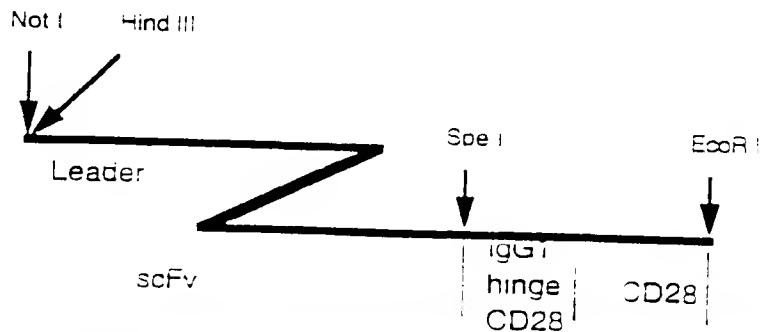
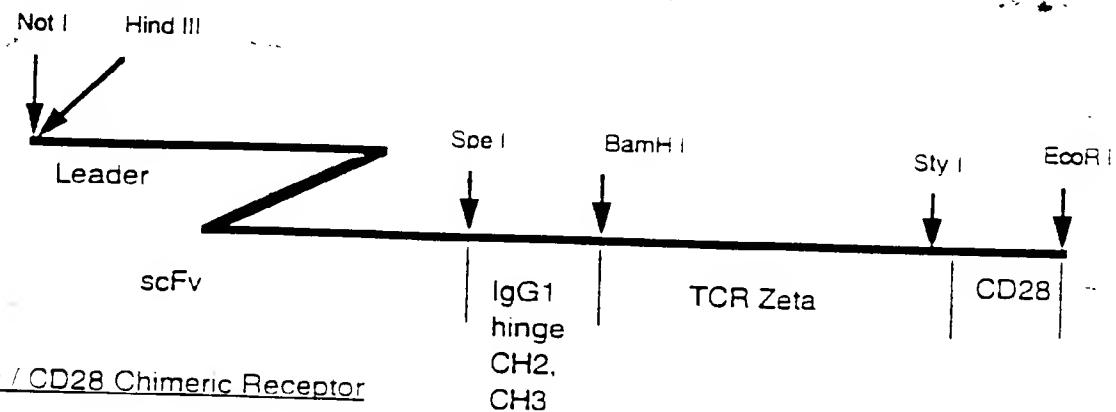
2140

FIG. 2a  
Construct cassettes cloned into pBluescript SK +

scFv / G1 / Zeta Chimeric Receptor



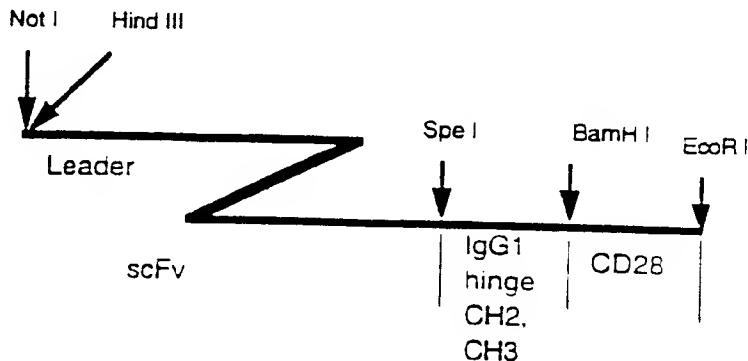
scFv / G1 / Zeta-CD28 fusion Chimeric Receptor



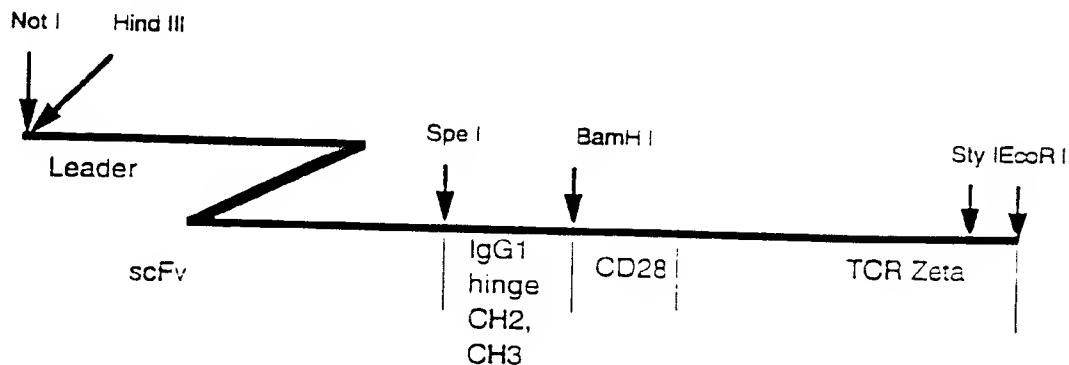
3/40

FIG. 2b  
Construct cassettes cloned into pBluescript SK +

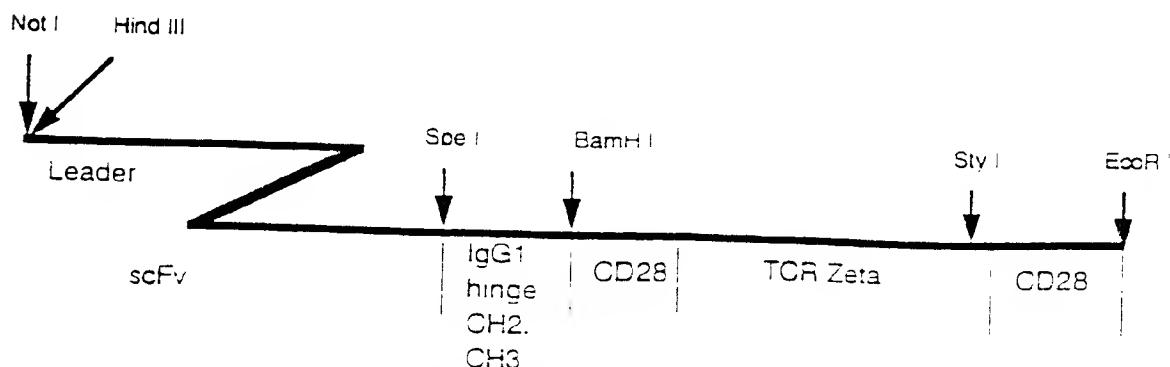
scFv /G1 /CD28 Chimeric Receptor



scFv /G1 /CD28-Zeta fusion Chimeric Receptor



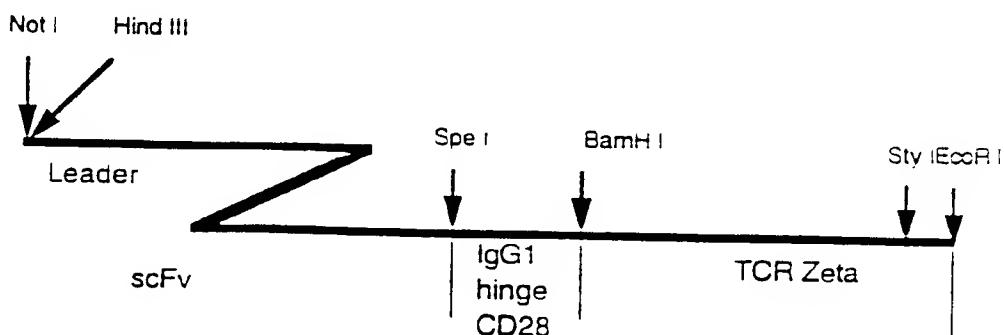
scFv /G1 /CD28-Zeta-CD28 fusion Chimeric Receptor



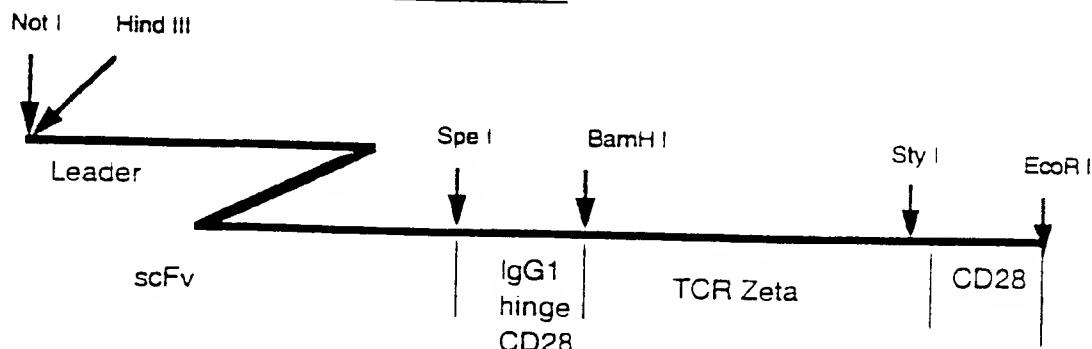
4 1:40

FIG. 2c  
Construct cassettes cloned into pBluescript SK +

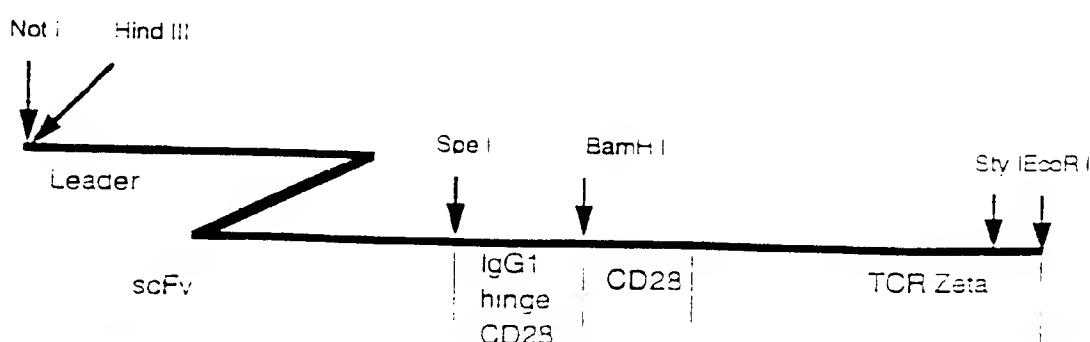
scFv / h.28 / Zeta Chimeric Receptor



scFv / h.28 / Zeta - CD28 fusion Chimeric Receptor



scFv / h.28 / CD28-Zeta fusion Chimeric Receptor



09/091608

WO 97/23613

PCT/GB96/03209

5/40

FIG. 3  
OLIGONUCLEOTIDE SEQUENCES FOR T-BODY CONSTRUCTION

All oligos listed in the 5' to 3' orientation.

R6490 : ATA TAG CGG CCG CAA GCT TCC ACC ATG TCT GTC CCC ACC CAA  
GTC CTC

R6491 : TGA CCC TCC GCC ACC TGA CCC TCC GCC ACC TGA CCC TCC GCC  
ACC TGA CCC TCC GCC ACC TGA CCC TCC GCC ACC TTT TAC TTC TAC TTT AGT ACC

R6492 : GGT GGC GGA GGG TCA GGT GGC GGA GGG TCA GGT GGC GGA  
GGG TCA GGT GGC GGA GGG TCA GAG GTG CAG CTG GTG CAG TCT

R6493 : TAT ATA CTA GTA GAA GAC ACT GTC ACC AGT

R6516 : TGA CCC TCC GCC ACC TGA CCC TCC GCC ACC TGA CCC TCC GCC  
ACC TGA CCC TCC GCC ACC CGT ACG TTT TAC TTC TAC TTT

R6515 : GGT GGC GGA GGG TCA GGT GGC GGA GGG TCA GGT GGC GGA  
GGG TCA GGT GGC GGA GGG TCA CAG ATT CAG CTG GTG CAG TCT

R6514 : TAT ATA CTA GTC GGG CCC TTC GTT GAG GCA

R6494 : ATA TAA CTA GTA ACT CCA TCA TGT ACT TCA GCC ACT TCG TGC  
CGG TCT TCC TGC CAG CG

R6495 : CGG TGT TGG TGG TCG CGG CGC TGG CGT CGT GGT GGG CTT CGC  
TGG CAG GAA GAC CGG CAC

R6496 : GCG CGG CGA CCA CCA ACA ACA CCG GCG CCC ACC ATC GCG TCG CAG  
CCC CTG TCC CTG CGC CCA

R6497 : TAT ATG GAT CCA GCA GGC CAA AGC TCT GCG CCT CTG GGC GCA  
GGG ACA GGG GCT G

R6506 : TAT ATG GAT CCC GCG TCT GGG CGC AGG GAC AGG GGC TG

R6486 : ATA TAG GAT CCC AAA CTC TGC TAC CTG CTG

6/40

## FIG. 3 (contd.)

R6489 : TAT ATG AAT TCT TAG CGA GGG GGC AGG GCC TGC AT

P3240 : TAT GGA TCC AAG CCC TTT TGG GTG CTG GTG GTG

P3241 : TAT GAA TTC TCA GGA GCG ATA GGC TGC GAA

P3301 : GCC ACC AAG GAC ACC TAC GAC GC

P3302 : CCC CCT CGC AGG AGT AAG AGG AGC AGG CTC CTG CAC AGT GAC  
TAC ATG AAC ATG ACT CCC C

P3303 : CAA GCA TTA CCA GCC CTA TGC CCC ACC ACG CGA CTT CGC AGC  
CTA TCG CTC CTG AGA ATT CAT A

P3304 : TAT GAA TTC TCA GGA GCG ATA G

P3305 : GCA TAG GGCTGG TAA TGC TTG CGG GTG GGC CCG GGG CGG CGG  
GGA GTC ATG TTC ATG TAG T

P3306 : CTC TTA CTC CTG CGA GGG GGC AGG GCC TGC ATG TGA AGG GCG  
TCG TAG GTG TCC TTG GTG GC

S0146 : CGA CTA GTG ACA AAA CTC ACA CAT GCC CAC CGT GCC CAA AAG  
GGA AAC ACC TTT GTC CAA GGT CCC

S0060 : CGA CTA GTG ACA AAA CTC ACA CAT GCC CAC CG

S0061 : TTG GGA TCC AGT TTA CCC GGA GAC AGG GAG AGG CT

T4057 : CTA CTA GTG ACA AAA CTC ACA C

T4058 : TTG GGA TCC AGG GGC TTA GAA GGT CCG GGA AAT AG

T7145 : CTG GAT CCC AAA TTT TGG GTG CTG GTG GTG GTT G

T4060 : GCT CCT GCT GAA CTT CAC TCT GGA GCG ATA GGC TGC GAA GTC G

T4387 : GCG ACT TCG CAG CCT ATC GCT CCA GAG TGA AGT TCA GCA GGA  
GCG

S4700 : TAT GAA TTC TTA GCG AGG GGG CAG GGC CTG CAT G

7/40

FIG. 4

SEQUENCE OF hCTM01 / CD8 / ZETA RECOMBINANT CHIMERIC RECEPTOR

10	20	30	40	
ATG TCT GTC CCC ACC CAA GTC CTC GGA CTC CTG CTG CTG TGG				
TAC AGA CAG GGG TGG GTT CAG GAG CCT GAG GAC GAC GAC ACC				
M S V P T Q V L G L L L W>				
50                    60                    70                    80				
CTT ACA GAT GCC AGA TGC GAT ATC CAG ATG ACT CAG AGT CCA				
GAA TGT CTA CGG TCT ACG CTA TAG GTC TAC TGA GTC TCA GGT				
L T D A R C D I Q M T Q S P>				
90                    100                    110                    120				
AGT ACT CTC AGT GCC AGT GTC GGT GAT AGG GTC ACC ATC ACT				
TCA TGA GAG TCA CGG TCA CAT CCA CTA TCC CAG TGG TAG TGA				
S T L S A S V G D R V T I T>				
130                    140                    150                    160				
TGT AGG AGT AGT AAA AGT CTC CTC CAT AGT AAC GGT GAC ACC				
ACA TCC TCA TCA TTT TCA GAG GAG GTC TCA TTY CCA CTG TGG				
C R S S K S L L H S N G D T>				
170                    180                    190                    200                    210				
TTC CTC TAT TGG TTC CAG CAG AAA CCA GGT AAA GCC CCA AAG				
AAG GAG ATA ACC AAG GTC GTC TTT GGT CCA TTT CGG GGT TTC				
F L Y W F Q Q K P G K A P K>				
220                    230                    240                    250				
CTC CTC ATG TAT AGG ATG AGT AAC CTC GCC AGT GGT GTC CCA				
GAG GAG TAC ATA TCC TAC TCA TTY GAG CGG TCA CCA CAT GGT				
L L M Y R M S N L A S G V P>				
260                    270                    280                    290				
TCT AGA TTC AGT GGT AGT GGT ACT GAG TTC ACT CTC				
AGA TCT AAG TCA CCA TCA CCA TCA TGA CTC AAG TGA GAG				
S R F S G S G S G T E F T L>				
300                    310                    320                    330				
ACT ATC AGT AGT CTC CAG CCA GAT GAT TTC GCC ACT TAT TAT				
TGA TAG TCA TCA GAG GTC GGT CTA CTA AAG CGG TGA ATA ATA				
T I S S L Q P D D F A T Y Y>				
340                    350                    360                    370				
TGT ATG CAG CAT CTC GAA TAT CCA TTC ACT TTC GGT CAG GGT				
ACA TAC CTC GTC GTC GAG CTT ATA GGT AAG TGA AAG CCA CTC CCA				
C M Q H L E Y P F T F G Q G>				
380                    390                    400                    410                    420				
ACT AAA GTC GAA GTC AAA CCT ACG GGT GCC GGA GGG TCA GGT				
TGA TTT CAT CTT CAT TTT CCA TGC CCA CGG CCT CGG ACT CCA				
T K V E Y K R T G G G G S G>				

09/091608

WO 97/23613

PCT/GB96/03209

8 / 40

FIG. 4 (contd.)

430 440 450 460  
GGC GGA GGG TCA GGT GGC GGA GGG TCA GGT GGC GGA GGG TCA  
CGG CCT CCC AGT CCA CGG CCT CCC AGT CCA CGG CCT CCC AGT  
G G G S G G G S G G G G S >  
470 480 490 500  
GGT GGC GGA GGG TCA CAG ATT CAG CTG GTG CAG TCT GGA GCA  
CCA CGG CCT CCC AGT GTC TAA GTC GAC CAC GTC AGA CCT CCT  
G G G S Q I Q L V Q S G A >  
510 520 530 540  
GAG GTG AAG AAG CCT GGA TCT TCT GTG AAG GTG TCT TGT AAG  
CTG CAC TTC TTC GGA CCT AGA AGA CAC TTC CAC AGA AGA AGA TTC  
E V K K P G S S V K V S C K >  
550 560 570 580  
GCA TCT GGA TAC ACC TTC ACC GAC TAC TAC ATT AAT TGG ATG  
CGT AGA CCT ATG TGG AAG TGG CTG ATG ATG TAA TTA ACC TAC  
A S G Y T F T D Y Y I N W M >  
590 600 610 620 630  
AGA CAG GCA CCT GGA CAG GGA CTC GAG TGG ATT GGA TGG ATT  
TCT GTC CGT GGA CCT GTC CCT GAG CTC ACC TAA CCT ACC TAA  
R Q A P G Q G L E W I G W I >  
640 650 660 670  
GAC CCT GGA TCT GGA AAT AGA AAG TAC AAT GAG AAG TTC AAG  
CTG GGA CCT AGA CCT TTA TGT TTC ATG TTA CTC TTC AAG TTC  
D P G S G N T K Y N E K F K >  
680 690 700 710  
GGA AGA GCA ACA CTG ACA GTG GAC ACA TCC ACG AAT ACC GGC  
CCT TCT CGT TCT GAC TCT CAC CTG TGT AGG TGC TTA TGG CGG  
G R A T L T V D T S T N T A >  
720 730 740 750  
TAC ATG GAG CTG TCT CCT AGA TCT GAG GAC ACA GCA TTC  
ATG TAC CTG GAC AGA AGA CAC TCT AGA CTC CTG TGT CGT AAG  
Y M E L S S L R S E S T T A F >  
760 770 780 790  
TAC TTC TCT GCA AGA GAG AAG AGG AGG TAC TAC GAC GCA ATG  
ATG AAG AGA ACA CCT TCT CTG TTC TGG TGG ATG ATG ATG CCT TAC  
Y F C A R E K T T Y Y Y A >  
800 810 820 830 840  
GAC TAC TGG GCA GAG GGA AGA CTC CTG GCA AGA GTC TCT TCT GGC  
CTG ATG AGC CCT CTG CCT TCT GAC CAC TCT GAC AGA AGA GGC  
D Y W G S Q G T S V F V C C A >  
SUBSTITUTE SHEET (RULE 26)

09/091608

WO 97/23613

PCT/GB96/03209

9/40

## FIG. 4 (contd.)

850	860	870	880	
TCA ACG AAG GGC CGG ACT ACT AAC TCC ATC ATG TAC TTC AGC AGT TCG TTC CGG GGC TCA TCA TTG AGG TAG TAC ATG AAG TCG S T K G P T S N S I M Y F S>				
890	900	910	920	
CAC TTC GTG CGG GTC TTC CTG CCA GCG AAG CCC ACC ACG ACG GTG AAG CAC CGC CAG AAG GAC GGT CGC TTC GGG TGG TGC TGC H F V P V F L P A K P T T T>				
930	940	950	960	
CCA GCG CGG CGA CCA CCA ACA CGG GCG CGG ACC ATC CGG TCG GGT CGC CGC CGT GGT GGT TGT CGC CGC GGG TGG TAG CGC ACC P A P R P P T P A P T I A S>				
970	980	990	1000	
CAG CCC CTG TCC CTG CGC CCA GAG GCG CAG AGC TTT GGC CTG GTC GGG GAC AGG GAC GCG GGT CTC CGC GTC TCG AAA CGG GAC Q P L S L R P E A Q S F G L>				
1010	1020	1030	1040	1050
CTG GAT CCC AAA CTC TGC TAC CTG CTG GAT GGA ATC CTC TTC GAC CTA CGG TTT GAG ACG ATG GAC GAC CTA CCT TAG GAG AAG L D P K L C Y L L D G I L F>				
1060	1070	1080	1090	
ATC TAT GGT GTC ATT CTC ACT GCC TTG TTC CTG AGA GTG AAG TAG ATA CCA CGG TAA GAG TCA CGG AAC AAG GAC TCT CAC TTC I Y G V I L T A L F L R V K>				
1100	1110	1120	1130	
TTC AGC AGG AGC CGA GAC CGC CGG GCG TAC CAG CAG CGC CAG AAG TCG TCC TCG CGT CTG CGG GGG CGC ATG GTC GTC CGG GTC F S R S A D A P A Y Q Q G Q>				
1140	1150	1160	1170	
AAC CAG CTG TAT AAC GAG CTC ATT CTA GGA CGA AGA GAG GAG TTG GTC GAG ATA TTG CTC GAG TTA GAT CCT CCT TCT CTC CTC N I L Y N E L N I G R R E E>				
1180	1190	1200	1210	
TAG GAT CCT TTG GAC AAG AGA CCT CGC CGG GAC CCT GAG ATG ATG CTA CGA AAC CTC TTG TCT GCA CGG CGG CTC CGA CTC TAC Y D V L D K R R G R D P E M>				
1220	1230	1240	1250	1260
GGG GGA AAG CGG AGA AGG AAC CCT CGG GAA CGG CGG TAC CCC CCT TTC CGC TTG TCG TTG TCG CGA CGC CCT CGG GAC ATG G C K P R R K N P I E S I Y>				

09/091608

WO 97/23613

PCT/GB96/03209

10/40

FIG. 4 (contd)

1270                    1280                    1290                    1300  
AAT GAA CTG CAG AAA GAT AAG ATG CGG GAG GCC TAC AGT GAG  
TTA CTT GAC GTC TTT CTA TTC TAC CGC CTC CGG ATG TCA CTC  
N E L Q K D K M A E A Y S E>  
1310                    1320                    1330                    1340  
ATT GGG ATG AAA GGC GAG CGC CGG AGG GGC AAG GGG CAC GAT  
TAA CCC TAC TTT CCG CTC GCG GCC TCC CCG TTC CCC GTG CTA  
I G M K G E R R R G K G H D>  
1350                    1360                    1370                    1380  
GGC CTT TAC CAG GGT CTC AGT ACA GCC ACC AAG GAC ACC TAC  
CCG GAA ATG GTC CCA GAG TCA TGT CCG TGG TTC CTG TGG ATG  
G L Y Q G L S T A T K D T Y>  
1390                    1400                    1410                    1420  
GAC GGC CTT CAC ATG CAG GGC CTG CCC CCT CGC TAA  
CTG CGG GAA GTG TAC CTC CGG GAC GGG GGA GCG ATT  
D A L H M Q A L P P R \*

11/40

## FIG. 5

SEQUENCE OF hCTM01 CD8 'Zeta-CD28 FUSION RECOMBINANT CHIMERIC RECEPTOR

10	20	30	40	
ATG TCT GTC CCC ACC CAA GTC CTC GGA CTC CTG CTG CTG TGG CTT ACA				
TAC AGA CAG GGG TGG GTT CAG GAG CCT GAG GAC GAC GAC ACC GAA TGT				
m s v p t q v l g 1 1 1 1 1 1 w 1 e>				
50	60	70	80	90
GAT GCC AGA TCC GAT ATC CAG ATG ACT CAG AGT CCA AGT ACT ACT CTC AGT				
CTA CGG TCT ACC CTA TAG GTC TAC TGA GTC TCA GGT TCA TGA GAG TCA				
d a r c D i Q M T Q S P S T L S>				
100	110	120	130	140
GCC AGT CTA GGT GAT AGG GTC ACC ATC ACT TGT AGG AGT AGT AAA AGT				
CGG TCA CAT CCA CTA TCC CAG TGG TAG TGA ACA TCC TCA TCA TTT TCA				
A S V G D R V T I T C R S S K S>				
150	160	170	180	190
CTC CTC CAT AGT AAC GGT GAC ACC TTC CTC TAT TGG TTC CAG CAG AAA				
GAG GAG GTA TCA TTG CCA CTG TGG AAG GAG ATA ACC AAG GTC GTC TTT				
L L H S N G D T F L Y W F Q Q K>				
200	210	220	230	240
CCA GGT AAA GCC CCA AAG CTC CTC ATG TAT AGG ATG AGT AAC CTC GCC				
GGT CCA TTT CGG GGT TTC GAG GAG TAC ATA TCC TAC TCA TTG GAG CGG				
P G K A P K L L M Y R M S N I A>				
250	260	270	280	
AGT GGT CTA CCA TCT AGA TTC AGT GGT AGT GGT ACT GAG TTC				
TCA CCA CAT GGT AGA TCT AAG TCA CCA TCA CCA TCA CCA TGA CTC AAG				
S G V P S R F S G S G S G T E F>				
290	300	310	320	330
ACT CTC ACT ATC AGT AGT CTC CAG CCA GAT GAT TTC GCC ACT TAT TAT				
TGA GAG TGA TAC TCA TCA GAG GTC GGT CTA CTA AAG CGG TGA ATA ATA				
T L T I S S L Q P D D F A T Y Y>				
340	350	360	370	380
TGT ATG CAG CAT CTC GAA TAT CCA TTC ACT TTC GGT CAG GGT ACT AAA				
ACA TAC GTC CTA GAG CTT ATA CGT AAG TCA AAG CCA GTC CCA TGA TTT				
C M Q H L E Y P F T F G Q G T K>				
390	400	410	420	430
GTA GAA CTA AAA CGT ACG GGT GGC GGA GGG TCA GGT GGC GGA GGG TCA				
CAT CTT CAT TTT CCA TCG CCA CGG CGT CGG AGT CCA CGG CGT CGG AGT				
V E Y K R T C G C G G G G G G G S>				

09/091608

WO 97/23613

PCT/GB96/03209

12 / 40

## FIG. 5 (contd.)

440                    450                    460                    470                    480  
 GGT GGC GGA GGG TCA GGT GGC GGA GGG TCA GGT GGC GGA GGG TCA CAG  
 CCA CCG CCT CCC AGT CCA CCG CCT CCC AGT CCA CCG CCT CCC AGT GTC  
 G G G G S G G G G S G G G G S Q>  
 490                    500                    510                    520  
 ATT CAG CTG GTG CAG TCT GGA GCA GAG GTG AAG AAG CCT GGA TCT TCT  
 TAA GTC GAC CAC GTC AGA CCT CGT CTC CAC TTC TTC GGA CCT AGA AGA  
 I Q L V Q S G A E V K K P G S S>  
 530                    540                    550                    560                    570  
 GTG AAG GTC TCT TGT AAG GCA TCT GGA TAC ACC TTC ACC GAC TAC TAC  
 CAC TTC GAC AGA AGA TTC CCT AGA CCT ATG TGG AAG TGG CTG ATG ATG  
 V K V S C K A S G Y T F T D Y Y>  
 580                    590                    600                    610                    620  
 ATT AAT TGG ATG AGA CAG GCA CCT GGA CAG GGA CTC GAG TGG ATT GGA  
 TAA TTA ACC TAC TCT GTC CGT GGA CCT GTC CCT GAG CTC ACC TAA CCT  
 I N W M R Q A P G Q G L E W I G>  
 630                    640                    650                    660                    670  
 TGG ATT GAC CCT GGA TCT GGA AAT ACA AAG TAC AAT GAG AAG TTC AAG  
 ACC TAA CTG GGA CCT AGA CCT TTA TGT TTC ATG TTA CTC TTC AAG TTC  
 W I D P G S G N T K Y N E K F K>  
 680                    690                    700                    710                    720  
 GGA AGA GCA ACA CTG ACA CTG GAC ACA TCC ACG AAT ACC GGC TAC ATG  
 CCT TCT CGT TGT GAC TGT CAC CTG TGT AGG TCC TTA TGG CGG ATG TAC  
 G R A T L T V D T S T N T A Y M>  
 730                    740                    750                    760  
 GAG CTG TCT TGT CTG AGA TCT GAG GAC ACA GCA TTC TAC TTC TGT GCA  
 CTC GAC AGA AGA GAC TCT AGA CTC CTG TGT CGT AAG ATG AAG AGA CCT  
 E L S S L R S E D T A F Y F C A>  
 770                    780                    790                    800                    810  
 AGA GAG AAG ACC ACC TAC TAC TAC GCA ATG GAC TAC TGG GGA CAG GGA  
 TCT CTC TTC TGG TGG ATG ATG ATG CGT TAC CTG ATG ACC CCT GTC CCT  
 R E K T T Y Y Y A M D Y W G Q G>  
 820                    830                    840                    850                    860  
 ACA CTG CTG ACA CTG TCT TGT CCT TCA ACG AAG GGC CGG ACT AGT AAC  
 TGT GAC GAC TGT CAC AGA AGA CGG AGT TGG TTC CGG GGC TGA TCA TTC  
 T L V T V S S A S T K G P T S N>  
 870                    880                    890                    900                    910  
 TCC ATC ATG TAC TTC AGC GAC TTC CTG CGG GTC TTC CTG CCA CGG AAG  
 AGG TAG TAC ATG AAG TGG CTG AAG GAC CGC CGG AAG GAC GGT CGG TTC  
 S I M Y F S H F V P V F L P A K>

09/091608

WO 97/23613

PCT/GB96/03209

13/40

## FIG. 5 (contd.)

920                    930                    940                    950                    960  
 CCC ACC ACG ACG CCA GCG CCG CGA CCA CCA ACA CGG CGG CCC ACC ATC  
 GGG TGG TGC TGC GGT CGC GGC GCT GGT GGT TGT TGT CGC CGC CGG TGG TAG  
 P T T T P A P R P P T P A P T I>  
  
 970                    980                    990                    1000  
 GCG TGG CAG CCC CTG TCC CTG CGC CCA GAG GCG CAG AGC TTT GGC CTG  
 CGC AGC GTC GGG GAC AGG GAC GCG GGT CTC CGC GTC TCG AAA CGG GAC  
 A S Q P L S L R P E A Q S F G L>  
  
 1010                   1020                   1030                   1040                   1050  
 CTG GAT CGC AAA CTC TCC TAC CTG CTG GAT CGA ATC CTC TTC ATC TAT  
 GAC CTA GGG TTT GAG ACG ATG GAC GAC CTA CCT TAG GAG AAG TAG ATA  
 L D P K L C Y I D G I L F I Y>  
  
 1060                   1070                   1080                   1090                   1100  
 GGT GTC ATT CTC ACT GCC TTG TTC CTG AGA GTG AAG TTC AGC AGG AGC  
 CCA CAG TAA GAG TGA CGG AAC AAG GAC TCT CAC TTC AAG TCG TCC TCG  
 G V I L T A L F L R V K F S R S>  
  
 1110                   1120                   1130                   1140                   1150  
 GCA GAC GCC CCC GCG TAC CAG CAG GGC CAG AAC CAG CTC TAT AAC GAG  
 CGT CTG CGG GGG CGC ATG GTC GTC CGG GTC TTG GTC GAG ATA TTG CTC  
 A D A P A Y Q Q G Q N Q L Y N E>  
  
 1160                   1170                   1180                   1190                   1200  
 CTC AAT CTA GGA CGA AGA GAG GAG TAC GAT GTT TTG GAC AAG AGA CCT  
 GAG TTA GAT CCT CCT TTT CTC CTC ATG CTA CAA AAC CTG TTC TCT CGA  
 L N L G R R E E Y D V L D K R R>  
  
 1210                   1220                   1230                   1240  
 GGC CGG GAC CCT GAG ATG GGG GGA AAG CGG AGA AGG AAG AAC CCT CAG  
 CGG CGC CTG GGA CTC TAC CGC CCT TTC GGC TCT TCC TTC TTG GGA GTC  
 G R D P E M G G K P R R K N P Q>  
  
 1250                   1260                   1270                   1280                   1290  
 GAA GGC CTG TAC AAT GAA CTG CAG AAA GAT AAG ATG GCG GAG GGC TAC  
 CTT CGG GAC ATG TTA CTT GAC GTC TTC CTA TTC TAC CGC CTC CGG ATG  
 E G I Y N E L Q K D K M A E A Y>  
  
 1300                   1310                   1320                   1330                   1340  
 AGT GAG ATT GGG ATG AAA CGC GAG CGG CGG AGG GGC AAG GGG CAC GAT  
 TCA CTC TAA CGC TAC TTT CGG CTC CGG CGC TCC CGG TTC CGG CGC CTC  
 S E I G M K G E R R B G X G H D>  
  
 1350                   1360                   1370                   1380                   1390  
 CGC CTT TAC CAG GGT CTC AGT ACA CGC AGC AAG GAC AGC TAC GAC CGC  
 CGG GAA ATG GTC CGA GAG TCA TGT CGG TGG TTC CTC TGG ATG CTC CGG  
 G I Y Q G L S T A T K D T Y D A>

09/091608

WO 97/23613

PCT/GB96/03209

14140

FIG.5 (contd.)

1400            1410            1420            1430            1440  
CTT CAC ATG CAG GCC CTG CCC CCT CGC AGG ACT AAG AGG AGC AGG CTC  
GAA GTG TAC GTC CGG GAC GGG GGA GCG TCC TCA TTC TCC TCG TCC GAG  
L   H   M   Q   A   L   P   P   R   R   S   K   R   S   R   L>  
1450            1460            1470            1480  
CTG CAC AGT GAC TAC ATG AAC ATG ACT CCC CCC CGC CCC GGG CCC ACC  
GAC GTG TCA CTG ATG TAC TTG TAC TGA GGG GCG GCG GGG CCC GGG TGG  
L   H   S   D   Y   M   N   M   T   P   R   R   P   G   P   T>  
1490            1500            1510            1520            1530  
CCC AAG CAT TAC CAG CCC TAT GCC CCA CCA CCC GAC TTC GCA GCC TAT  
GGG TTC GTA ATG GTC GGG ATA CGG GGT GGT GCG CTG AAG CGT CGG ATA  
R   K   H   Y   Q   P   Y   A   P   P   R   D   F   A   A   Y>  
1540  
CCC TCC TGA  
GGG AGG ACT  
R   S   \*  
-

09/091608

WO 97/23613

PCT/GB96/03209

15/40

FIG. 6

SEQUENCE OF hCTM01 /CD8 / CD28 RECOMBINANT CHIMERIC RECEPTOR

10	20	30	40	
ATG TCT GTC CCC ACC CAA GTC CTC GGA CTC CTG CTG CTG CTG TGG				
TAC AGA CAG GGG TGG GTT CAG GAG CCT GAG GAC GAC GAC GAC ACC				
M S V P T Q V L G L L L L W>				
50                    60                    70                    80				
CTT ACA GAT CCC AGA TGC GAT ATC CAG ATG ACT CAG AGT CCA				
GAA TGT CTA CGG TCT ACG CTA TAG GTC TAC TGA GTC TCA GGT				
L T D A R C D I Q M T Q S P>				
90                    100                    110                    120				
AGT ACT CTC AGT CCC AGT GTA GGT GAT AGG GTC ACC ATC ACT				
TCA TGA GAG TCA CGG TCA CAT CCA CTA TCC CAG TGG TAG TGA				
S T L S A S V G D R V T I T>				
130                    140                    150                    160				
TGT AGG AGT AGT AAA AGT CTC CTC CAT AGT AAC GGT GAC ACC				
ACA TCC TCA TCA TTT TCA GAG GAG GTA TCA TTG CCA CTG TGG				
C R S S K S L L H S N G D T>				
170                    180                    190                    200                    210				
TTC CTC TAT TGG TTC CAG CAG AAA CCA GGT AAA GCC CCA AAG				
AAG GAG ATA ACC AAG GTC GTC TTT GGT CCA TTT CGG GGT TTC				
F L Y W F Q Q K P G K A P K>				
220                    230                    240                    250				
CTC CTC ATG TAT AGG ATG AGT AAC CTC CCC AGT GGT GTA CCA				
GAG GAG TAC ATA TCC TAC TCA TTG GAG CGG TCA CCA CAT GGT				
L L M Y R M S N L A S G V P>				
260                    270                    280                    290				
TCT AGA TTC AGT GGT AGT GGT AGT ACT GAG TTC ACT CTC				
AGA TCT AAG TCA CCA TCA CCA TCA CCA TGA CTC AAG TGA GAG				
S R F S G S G S G T E F T L>				
300                    310                    320                    330				
ACT ATC AGT AGT CTC CAG CCA GAT GAT TTC GGC ACT TAT TAT				
TGA TAG TCA TCA GAG GTC GGT CTC CTC AAG CGG TCA ATA ATA				
T I S S L Q P D S F A T Y Y>				
340                    350                    360                    370				
TGT ATG CAG CAT CTC GAA TAT CCA TTC ACT TTC GGT CAG CGT				
ACA TAC CTC CTC GAG CTT ATA CGT AAG TCA AAG CCA GTC CGT				
C M Q H L E V P F T F S I G>				

09/091608

WO 97/23613

PCT/GB96/03209

16 / 40

## FIG. 6 (contd.)

380	390	400	410	420
ACT AAA GCA GAA GCA AAA CGT ACG GGT GGC GGA GGG TCA GGT				
TGA TTT CAT CTT CAT TTT GCA TGC CCA CCG CCT CCC AGT CCA				
T K V E V K R T G G G G S G >				
430	440	450	460	
GGC GGA CGG TCA GGT GGC GGA CGG TCA GGT GGC GGA CGG TCA				
CCG CCT CCC AGT CCA CGG CCT CCC AGT CCA CGG CCT CCC AGT				
G G G S G G G S G G G S G G G S >				
470	480	490	500	
GGT GGC GGA CGG TCA CAG ATT CAG CTG GTG CAG TCT GGA GCA				
CCA CGG CCT CCC AGT GTC TAA GTC GAC CAC CTG AGA CCT CGT				
G G G S Q I Q L V Q S G A >				
510	520	530	540	
GAG GTG AAG AAG CCT GGA TCT TCT GTG AAG GTG TCT TGT AAG				
CTG CAC TTC TTC GGA CCT AGA AGA CAC TTC CAC AGA ACA TTC				
E V K K P G S S V K V S C K >				
550	560	570	580	
GCA TCT GGA TAC ACC TTC ACC GAC TAC TAC ATT AAT TGG ATG				
CGT AGA CCT ATG TGG AAG TGG CTG ATG ATG TAA TTA ACC TAC				
A S G Y T F T D Y Y I N W M >				
590	600	610	620	630
AGA CAG GCA CCT CGA CAG GCA CTG GAG TGG ATT GGA TGG ATT				
TCT GTG CGT GGA CCT GTC CCT GAG CTG ACC TAA CCT ACC TAA				
R Q A P G Q G L E W I G W I >				
640	650	660	670	
GAC CCT GGA TCT GGA AAT ACA AAG TAC AAT GAG AAG TTC AAG				
CTG GGA CCT AGA CCT TTA TGT TTC ATG TTA CTG TTC AAG TTC				
D P G S G N T K Y N E K F K >				
680	690	700	710	
GGA AGA GCA ACA CTG ACA GTG GAC ACA TGG ACG AAT ACC GGC				
CCT TCT CGT TGT GAC TGT GAC CTG TGT ACG TGG TWA TGG CGG				
G R A T L T V D T S T N C A >				
720	730	740	750	
TAC ATG GAG TTC TGT TCT CTG AGA TGT GAG GAG AGA GCA TTC				
ATG TAC CTG GAC AGA AGA GAC TGT AGA GCA CTG CTG TGT CCT AAG				
Y M E L S S L R S E D T A F >				
760	770	780	790	
TAC TTC TGT GCA AGA GAG AAG ACC ACC TAC TAC TAC GCA ATG				
ATG AAG AGA CCT TGT CTG TTC TGG TGG ATG ATG ATG CCT TAC				
Y F E A S E K T T Y Y M A M >				

09/091608

WO 97/23613

PCT/GB96/03209

17/40

## FIG. 6 (contd.)

800	810	820	830	840
GAC TAC TGG GGA CAG GGA ACA CTG GTG ACA GTG TCT TCT GCC CTG ATG ACC CCT GTC CCT TGT GAC CAC TGT CAC AGA AGA CGG D Y W G Q G T L V T V S S A>				
850	860	870	880	
TCA ACG AAG GGC CCG ACT AGT AAC TCC ATC ATG TAC TTC AGC AGT TGC TTC CCG GGC TGA TCA TTG AGG TAG TAC ATG AAG TCG S T K G P T S N S I M Y F S>				
890	900	910	920	
CAC TTC GTG CCG GTC TTC CTG CCA GCG AAG CCC ACC ACG ACG GTG AAG CAC GGC CAG AAG GAC GGT CGC TTC GGG TGG TGC TGC H F V P V F L P A K P T T T				
930	940	950	960	
CCA GCG CCG CGA CCA CCA ACA CCG GCG CCC ACC ATC GCG TCG GGT CGC GGC GCT GGT GGT TGT GGC CGC GGG TGG TAG CGC AGC P A P R P P T P A P T I A S>				
970	980	990	1000	
CAG CCC CTG TCC CTG CGC CCA GAG GCG GGA TCC AAG CCC TTT GTC GGG GAC GAC GCG GGT CTC CGC CCT AGG TTC GGG AAA Q P L S L R P E A G S K P F>				
1010	1020	1030	1040	1050
TGG GTG CTG GTG GTG GTT GGT GGA GTC CTG GCT TGC TAT AGC ACC CAC GAC CAC CAA CCA CCT CAG GAC CGA AGG ATA TCG W V L V V V G G V L A C Y S>				
1060	1070	1080	1090	
TTG CTA GTA ACA GTG GGC TTT ATT ATT TTC TGG GTG AGG AGT AAC GAT CAT TGT CAC CGG AAA TAA TAA AAG ACC CAC TCC TCA L L V T V A F I I F W V R S>				
1100	1110	1120	1130	
AAG AGG AGC AGG CTC CTG CAC AGT GAC TAC ATG AAC ATG ACT TTC TCC TCG TCC GAG GAC CTG TCA CTG ATG TAC TTG TAC TGA K R S R L L H S D Y M N M T>				
1140	1150	1160	1170	
CCC CGG CGG CGG GGG CGG ACC CGG AAG CAT TAC CAG CGG TAT GGG CGG CGG CGG CGG TGG CGG TTC GTA ATG GTC CGG ATA P R R P C P T R K H Y Q P Y>				
1180	1190	1200	1210	
CCC CGA CGA CGG GAC TTC GCA CGG TAT CGG TCG TGA CGG CGT CGT CGG CGG AAG CGT CGG ATA CGG AGG ACT A P P R D F A A Y R S *				

09/091608

WO 97/23613

PCT/GB96/03209

18140

FIG. 7

SEQUENCE OF hCTM01 / G1 / ZETA RECOMBINANT CHIMERIC RECEPTOR

09/091608

WO 97/23613

PCT/GB96/03209

19 / 40

## FIG. 7 (contd.)

440 \* 450 \* 460 \* 470 \* 480 \*  
 GGT GGC GGA GGG TCA GGT GGC CGA GGG TCA GGT GGC GGA GGG TCA CAG  
 CCA CCG CCT CCC AGT CCA CCG CCT CCC AGT CCA CCG CCT CCC AGT GTC  
 G G G G S G G G S G G G G S Q>  
  
 490 \* 500 \* 510 \* 520 \*  
 ATT CAG CTG GTG CAG TCT CGA GCA GAG GTG AAG AAG CCT GGA TCT TCT  
 TAA GTC GAC CAC GTC AGA CCT CGT CTC CAC TTC TTC GGA CCT AGA AGA  
 I Q L V Q S G A E V K K P G S S>  
  
 530 \* 540 \* 550 \* 560 \* 570 \*  
 GTG AAG GTG TCT TGT AAG GCA TCT GGA TAC ACC TTC ACC GAC TAC TAC  
 CAC TTC CAC AGA ACA TTC CGT AGA CCT ATG TGG AAG TGG CTG ATG ATG  
 V K V S C K A S G Y T F T D Y Y>  
  
 580 \* 590 \* 600 \* 610 \* 620 \*  
 ATT AAT TGG ATG AGA CAG GCA CCT GGA CAG GGA CTC GAG TGG ATT GGA  
 TAA TTA ACC TAC TCT GTC CGT GGA CCT GTC CCT GAG CTC ACC TAA CCT  
 I N W M R Q A P G Q G L E W I G>  
  
 630 \* 640 \* 650 \* 660 \* 670 \*  
 TGG ATT GAC CCT GGA TCT GGA AAT ACA AAG TAC AAT GAG AAG TTC AAG  
 ACC TAA CTG GGA CCT AGA CCT TTA TGT TTC ATG TTA CTC TTC AAG TTC  
 W I D P G S G N T K Y N E K F K>  
  
 680 \* 690 \* 700 \* 710 \* 720 \*  
 CGA AGA CGA AGA CTG AGA CTG GAC AGA TCC ACC AAT ACC CGG TAC ATG  
 CCT TCT CCT TGT GAC TGT CAC CTG TGT AGG TGG TTA TGG CGG ATG TAC  
 G R A T L T V D T S T N T A Y M>  
  
 730 \* 740 \* 750 \* 760 \*  
 GAG CTG TCT TGT CTG AGA TCT GAG GAC ACA GCA TTC TAC TTC TGT GCA  
 CTC GAC AGA AGA GAC TCT AGA CTC CTG TGT CGT AAG ATG AAG AGA CCT  
 E L S S L R S E D T A F Y F C A>  
  
 770 \* 780 \* 790 \* 800 \* 810 \*  
 AGA GAG AAG ACC ACC TAC TAC GCA ATG GAC TAC TGG GGA CGG GGA  
 TCT CTC TTC TGG TGG ATG ATG ATG CGT TAC CTG ATG ACC CCT CGT CCT  
 R E K T T Y Y Y A M D Y W G Q G>  
  
 820 \* 830 \* 840 \* 850 \* 860 \*  
 ACA CTG GTG AGA CTG TCT TGT GGC TCA AGG AAG GGC CGG ACT AGT GAC  
 TGT GAC GAC TGT GAC AGA AGA CGG AGT TGC TTC CGG GGC TGA TCA CTG  
 T L V T V S S A S T K G P T S D>  
  
 870 \* 880 \* 890 \* 900 \* 910 \*  
 AAA ACT CGC AGA TGG CGA CGG TGC CGA GCA CCT GAA CTG CTG CGG CGA  
 TTT TGA GTG TCT AGG GGT CGG AGG CCT CGT CGA CGG CGT CGT CGA CGC CGT  
 K T H T C P P C P A P S L L S G>

09/091608

WO 97/23613

PCT/GB96/03209

20/40

## FIG. 7 (contd.)

920            930            940            950            960  
 CCG TCA GTC TTC CTC TTC CCC CCA AAA CCC AAG GAC ACC CTC ATG ATC  
 GGC AGT CAG AAG GAG AAG GGG GGT TTT GGG TTC CTC TCG TCG GAG TAC TAG  
 P S V F L F P P K P K D T L M I>  
  
 970            980            990            1000  
 TCC CGG ACC CCT GAG GTC ACA TGC GTG GTG GAC GTG ACC CAC GAA  
 AGG GCC TGG GGA CTC CAG TGT ACG CAC CAC CAC CTC CAC TCG GTG CTT  
 S R T P E V T C V V V D V S H E>  
  
 1010           1020           1030           1040           1050  
 GAC CCT GAG GTC AAG TTC AAC TGG TAC GTG GAC GGC GTG GAG GTG CAT  
 CTG GGA CTC CAG TTC AAG TTC ACC ATG CAC CTG CCG CAC CTC CAC GTC  
 D P E V K F N W Y V D G V E V H>  
  
 1060           1070           1080           1090           1100  
 AAT GGC AAG ACA AAG CCC CCC GAG GAG CAG TAC AAC AGC AGC TAC CGT  
 TTA CGG TTC TGT TTC GGC GCC CTC CTC GTC ATG TTG TCG TGC ATG GCA  
 N A K T K P R E E Q Y N S T Y R>  
  
 1110           1120           1130           1140           1150  
 GTG GTC ACC GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG AAT GGC AAG  
 CAC CAG TCG CAG GAG TGG CAG GAC GTG GTC CTG ACC GAC TTA CCG TTC  
 V V S V L T V L H Q D W L N G K>  
  
 1160           1170           1180           1190           1200  
 GAG TAC AAG TGC AAG GTC TCC AAC AAA GGC CTC CCA GGC CCC ATC GAG  
 CTC ATG TTC ACG TTC CAG AGG TTG TTT CGG GAG GGT CGG GGG TAG CTC  
 E Y K C K V S N K A L P A P I E>  
  
 1210           1220           1230           1240  
 AAA ACC ATC TCC AAA GGC AAA GGG CAG CCC CCA GAA CCA CAG GTG TAC  
 TTT TGG TAG AGG TTT CGG TTT CCC GTC GGG GGT CTT GGT GTC CAC ATG  
 K T I S K A K G Q P R E P Q V Y>  
  
 1250           1260           1270           1280           1290  
 ACC CTG CCC CCA TCC CCG GAG GAG ATG ACC AAC AAC CAG GTC AGC CTC  
 TGG GAC GGG GGT AGG GGC CTC CTC TAC TGG TTC TTG GTC CAG TCG GAC  
 T L P P S R E E M T K N Q V S L>  
  
 1300           1310           1320           1330           1340  
 ACC TGC CTG GTC AAA GGC TTC TAT CCC AGC GAC ATG GTC GGC GTC GAG TGG  
 TGG AGG GAC CAG TTT CGG AAG ATA GGG TGG CTC TAG CGG CAC CTC ACC  
 T C L V K G F Y P S D I A V E W>  
  
 1350           1360           1370           1380           1390  
 GAG ACC AAT GGG CAG CCC GAG AAC AAC TAC AAC AAG ACC ACC CCT CCC CTG  
 CTC TCG TTA CCC GTC GGC CTC TTG TTG ATG TTC TGG TGC CGA CGG CAC  
 E S N G Q P E N N Y K T T P S V Y>  
  
 1400           1410           1420           1430           1440  
 CTG GAC TCC GAC CCC TCC TTC TTC CTC TAC ACC AAC AAC CTC ACC GTC GAC  
 GAC CTC AGG CTC CCG AGG AAC AAC GAG ATG TCC TTC GAG TGG CAC CGC  
 L D S D G S F F L Y S K L T V D>

09/091608

WO 97/23613

PCT/GB96/03209

## 21/40 FIG. 7 (contd.)

1450                    1460                    1470                    1480  
 AAG AGC AGG TCG CAG CAG GGG AAC GTC TTC TCA TGC TCC TCG ATG CAT  
 TTC TCG TCC ACC GTC GTC CCC TTG CAG AAG ACT ACG AGG GAC TAC GTC  
 K S R W Q Q G N V F S C S V M H>  
 1490                    1500                    1510                    1520                    1530  
 GAG GCT CTG CAC AAC CAC TAC ACG CAG AAG AGC CTC TCC CTG TCT CCG  
 CTC CGA GAC GTC TTG GTC ATG TGC GTC TTC TCG GAG AGG GAC AGA GGC  
 E A L H N H Y T Q K S L S L S P>  
 1540                    1550                    1560                    1570                    1580  
 GGT AAA CTG GAT CCC AAA CTC TGC TAC CTG CTG GAT GGA ATC CTC TTC  
 CCA TTT GAC CTA GGG TTT GAG ACG ATG GAC GAC CTA CCT TAG GAG AAG  
 G K L D P K L C Y L L D G I L F>  
 1590                    1600                    1610                    1620                    1630  
 ATC TAT CGT GTC ATT CTC ACT GCG TTG TTC CTG ATG AGA GTC AAG TTC AGC  
 TAG ATA CCA CAG TAA GAG TCA CGG AAC AAG GAC TCT CAC TTC AAG TCG  
 I Y G V I L T A L F L R V K F S>  
 1640                    1650                    1660                    1670                    1680  
 AGG AGC GCA GAC GCG CCC GCG TAC CAG CAG GGC CAG AAC CAG CTC TAT  
 TCC TCG CGT CTG CGG CGG CGC ATG GTC GTC CGG GTC TTG GTC GAG ATA  
 R S A D A P A Y Q Q G Q N Q L Y>  
 1690                    1700                    1710                    1720  
 AAC GAG CTC AAT CTA GGA CGA AGA GAG GAG TAC GAT GAT GTT TTG GAC AAG  
 TTG CTC GAG TTA GAT CCT GCT TCT CTC CTC ATG CTA CAA AAC CTG TTC  
 N E L N L G R R E E Y D V L D K>  
 1730                    1740                    1750                    1760                    1770  
 AGA CGT GGC CGG GAC CCT GAG ATG CGG CGA AAG CGG AGA AGG AAG AAC  
 TCT GCA CGG CGC CTG CGG CTC TAC CGG CCT TCT TTC GGC TCT TCC TTC TTG  
 R R G R D P E M G G K P R R K N>  
 1780                    1790                    1800                    1810                    1820  
 CCT CAG GAA CGC CTG TAC AAT GAA CTG CAG AAA GAT AAG ATG GCG GAG  
 GGA GTC CTT CGG GAC ATG TTA CTT GAC GTC TTT CTA TTC TAC CGC CTC  
 P Q E G L Y N E L Q K D K M A E>  
 1830                    1840                    1850                    1860                    1870  
 CGC TAC AGT GAG ATT CGG ATG AAA CGC GAG CGC CGG AGG GGC AAG CGG  
 CGG ATG TCA CTC TAA CGG TAC TTT CGG CTC CGG GCG TCC CGG TTG CGC  
 A Y S E I G M K G S R R R G K S>  
 1880                    1890                    1900                    1910                    1920  
 CAC GAT CGC CTT TAC CAG GGT CTC AGT AGA CGC ACC AAG GAC ACC TAC  
 GTG CTA CGG GAA ATG GTC CCA GAG TCA TCT CGG TGG TTC CGG TGG ATG  
 H D G I Y Q G L S T A T K D T Y>  
 1930                    1940                    1950  
 GAC CGC CTT CGC AGC ATG CAG CGC CTG CGG CCT CGC TAA  
 CTG CGG GAA GTG TAC GTC CGG GAC CGG GGA CGG ATT  
 D A L H M Q A L P P R

09/091608

WO 97/23613

PCT/GB96/03209

22 / 40

**FIG. 8**  
**SEQUENCE OF hCTM01/G1/ZETA-CD28 FUSION RECOMBINANT**  
**CHIMERIC RECEPTOR**

09/091608

WO 97/23613

PCT/GB96/03209

23/40

## FIG. 8 (contd.)

440 \* 450 \* 460 \* 470 \* 480  
 GGT GGC GGA GGG TCA GGT GGC GGA GGG TCA GGT GGC GGA GGG TCA CAG  
 CCA CGG CCT CCC AGT CCA CGG CCT CCC AGT CCA CGG CCT CCC AGT GTC  
 G G G G S G G G S G G G G G S Q>  
 490 \* 500 \* 510 \* 520  
 ATT CAG CTG GTG CAG TCT GGA GCA GAG GTG AAG AAG CCT GGA TCT TCT  
 TAA GTC GAC GAC CTG AGA CCT CGT CTC CAC TTC TTC GGA CCT AGA AGA  
 I Q L V Q S G A E V K K P G S S>  
 530 \* 540 \* 550 \* 560 \* 570  
 GTG AAG GTG TCT TGT AAG GCA TCT GGA TAC ACC TTC ACC GAC TAC TAC  
 CAC TTC CAC AGA AGA TTC CGT AGA CCT ATG TGG AAG TGG CTG ATG ATG  
 V K V S C K A C G Y T F T D Y Y>  
 580 \* 590 \* 600 \* 610 \* 620  
 ATT AAT TGG ATG AGA CAG GCA CCT GGA CAG GGA CTC GAG TGG ATT GGA  
 TAA TTA ACC TAC TCT GTC CGT GGA CCT GTC CCT GAG CTC ACC TAA CCT  
 I N W M R Q A P G Q G L E W I G>  
 630 \* 640 \* 650 \* 660 \* 670  
 TGG ATT GAC CCT GGA TCT GGA AAT ACA AAG TAC AAT GAG AAG TTC AAG  
 ACC TAA CTG GGA CCT AGA CCT TTA TGT TTC ATG TTA CTC TTC AAG TTC  
 W I D P G S G N T K Y N E K F K>  
 680 \* 690 \* 700 \* 710 \* 720  
 GGA AGA GCA ACA CTC ACA GTG GAC ACA TCC ACG AAT ACC GGC TAC ATG  
 CCT TCT CGT TGT GAC TGT CAC CTC TGT AGG TCC TTA TGG CGG ATG TAC  
 G R A T L T Y I T S T N T A Y M>  
 730 \* 740 \* 750 \* 760  
 GAG CTG TCT TCT CTG AGA TCT GAG GAC ACA GCA TTC TAC TTC TGT GCA  
 CTC GAC AGA AGA GAC TCT AGA CTC CTG TGT CGT AAG ATG AAG ACA CGT  
 E L S S L R S E D T A F Y F C A>  
 770 \* 780 \* 790 \* 800 \* 810  
 AGA GAG AAG ACC ACC TAC TAC TAC GCA ATG GAC TAC TGG GGA CAG GGA  
 TCT CTC TTC TGG TGG ATG ATG ATG CGT TAC CTC ATG ACC CCT GTC CCT  
 R E K T T Y Y Y A M S Y W G S G>  
 820 \* 830 \* 840 \* 850 \* 860  
 ACA CTG CTG AGA CTG TCT TCT GGC TCA ACG AAG GGC CGG ACT ACT GAC  
 TGT GAC GAC TCT GAC AGA AGA CGG ACT TGC TTC CGG CGG TGA TCA CTC  
 T L V T V S S A S T K G P T S D>  
 870 \* 880 \* 890 \* 900 \* 910  
 AAA ACT GAC AGA TCC GCA CGG TCG CCA GCA CGT GAA CTC CTC GGG GGA  
 TCT TGA CTG TGT AGG CGT CGG AGG CGT CGT GCA CGT GAG GAC CGG CCT  
 K T H T C P P C P A P E L L S S>

09/091608

WO 97/23613

PCT/GB96/03209

24/40  
FIG. 8 (contd.)

920	930	940	950	960
CCG TCA GTC TTC CTC TTC CCC CCA AAA CCC AAG GAC ACC CTC ATG ATC GGC AGT CAG AAG GAG AAG GGG GGT TTT GGG TTC CTC TCG GAG TAC TAG P S V F L F P P K P K D T L M I>				
970	980	990	1000	
TCC CGG ACC CCT GAG GTC ACA TGC GTG GTG GAC GTG AGC CAC GAA AGG GCC TGG GGA CTC CAG TGT ACG CAC CAC CAC CTG CAC TCG GTG CTT S R T P E V T C V V V D V S H E>				
1010	1020	1030	1040	1050
GAC CCT GAG GTC AAG TTC AAC TGG TAC GTG GAC CCC GTG GAG GTG CAT CTG GGA CTC CAG TTC AAG TTG ACC ATG CAC CTG CCG CAC CTC CAC GTA D P E V K F N W Y V D G V E V H>				
1060	1070	1080	1090	1100
AAT GCC TAG ACA AAG CCG CGG GAG GAG CAG TAC AAC ACC ACG TAC CGT TTA CGG TTC TGT TTC CGC CCC CTC CTC GTC ATG TTG TCG TGC ATG GCA N A K T K P R E E Q Y N S T Y R>				
1110	1120	1130	1140	1150
GTG GTC AGC GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG AAT GGC AAG CAC CAG TCG CAG GAG TGG CAG GAC GTG GTC CTG ACC GAC TTA CCG TTC V V S V L T V L H Q D W L N G K>				
1160	1170	1180	1190	1200
GAG TAC AAG TGC AAG GTC TCC AAC AAA GCC CCT CCA GGC CCC ATC GAG CTC ATG TTC ACG TTC CAG AGG TTG TTT CGG GAG GGT CGG GGG TAG CTC E Y K C K V S N K A L P A P I E>				
1210	1220	1230	1240	
AAA ACC ATC TCC AAA GCC AAA GGG CAG CCC CGA GAA CCA CAG GTG TAC TTT TGG TAG AGG TTT CGG TTT CCC GTC CGG GCT CTT GGT GTC CAC ATG K T I S K A K G Q P R E P Q V Y Y>				
1250	1260	1270	1280	1290
ACC CTG CCC CCA TCC CGG GAG GAG ATG ACC AAG AAC CAG GTC AGC CTG TGG GAC CGG GGT AGG GCC CTC CTC TAC TGG TTC TTG GTC CAG TCG GAC T L P P S R E E M T K N Q V S L>				
1300	1310	1320	1330	1340
ACC TCC CTG GTC AAA GCC TTC TAT CCC AGC GAC ATC GGC GTG GAG TGG TGG AGG GAC CGG TTT CGG AAG ATA CGG TCG CTG TAG CGG GAC CTC ACC T C I V K G F Y P S D I A V E W>				
1350	1360	1370	1380	1390
GAG AGC ATT CGG CAG CCC GAG AAC AAC TAC AAG ACC AGG CCT CCC GTG CTG TGG TTA CGG CTC CGG CTC TTC TTG ATG TTC TGG TCG CGA GGG GAC E S N G P E N N Y K T T P P V>				
1400	1410	1420	1430	1440
CTG GAC TGG GAC CGG TCC TTC TTC CTC TAC AGC AAG GTC ACC GTC GAC GAC GTC AGG CGG CGG AGG AAG AAG GAG ATG TGG TTC GAG TGG GAC CGG L D S D G S F P L Y S K D T V D>				

09/091608

WO 97/23613

PCT/GB96/03209

25/40  
FIG 8 (contd.)

1450 1460 1470 1480  
AAG AGC AGG TCG CAG CAG GGG AAC CTC TTC TCA TGC TCC GTG ATG CAT  
TTC TCG TCC ACC CTC GTC CCC TTG CAG AAG AGT ACG AGG CAC TAC GTC  
K S R W Q Q G N V F S C S V M H>  
1490 1500 1510 1520 1530  
GAG GCT CTG CAC AAC CAC TAC ACG CAG CAG AAG AGC CTC TCC CTG TCT CCC  
CTC CGA GAC GTG TTG GTG ATG TGC GTC TTC TCC GAG AGG GAC AGA GGC  
E A L H N H Y T Q K S L S L S P>  
1540 1550 1560 1570 1580  
GGT AAA CTG GAT CCC AAA CTC TGC TAC CTG CTG GAT GGA ATC CTC TTC  
CCA TTT GAC CTA GGG TTT GAG ACG ATG GAC GAC CTA CCT TAG GAG AAG  
G K L D P K L C Y L I D G I L F>  
1590 1600 1610 1620 1630  
ATC TAT GGT GTC ATT CTC ACT GCC TTG TTC CTG AGA GTG AAG TTC AGC  
TAG ATA CCA CAG TAA GAG TGA CGG AAC AAG GAC TCT CAC TTC AAG TCG  
I Y G V I L T A L F L R V K F S>  
1640 1650 1660 1670 1680  
AGG AGC GCA GAC GCC CCC GCG TAC CAG CAG GGC CAG AAC CAG CTC TAT  
TCC TCG CGT CTG CGG CCC ATG GTC GTC CGG GTC TTG GTC GAG ATA  
R S A D A P A Y Q Q G Q N Q L Y>  
1690 1700 1710 1720  
AAC GAG CTC AAT CTA GGA CGA AGA GAG GAG TAC GAT GTT TTG GAC AAG  
TTG CTC GAG TTA GAT CCT CCT TCT CTC CTC ATG CTA CAA AAC CTG TTC  
N E L N L G R R E E Y D V L D K>  
1730 1740 1750 1760 1770  
AGA CGT CGC CGG GAC CCT GAG ATG GGG GGA AAG CGG AGA AGG AAG AAC  
TCT GCA CGG CGC CTG GGA CTC TAC CCC CCT TTC CGC TCT TCG TTC TTG  
R R G R D P E M G G K P R R K N>  
1780 1790 1800 1810 1820  
CCT CAG GAA CGG CTG TAC AAT GAA CTG CAG AAA GAT AAG ATG GCG GAG  
GGA GTC CTT CGG GAC ATG TTA CTT GAC GTC TTT CTA TTC TAC CGC CTC  
P Q E G L Y N S L Q K D K M A E>  
1830 1840 1850 1860 1870  
GCC TAC AGT GAG ATT CGG ATG AAA CGC GAG CGG CGG AGG CGC AAG CGG  
CGG ATG TCA CGC TAA CGG TAC TTT CGG CTC CGG CGG TCG CGG CGG CGC  
A Y S E I G M K G E P R R G M G>  
1880 1890 1900 1910 1920  
CAC GAT CGC CTT TAC CAG CGT CTC AGT AGA CGC ACC AAG GAG AGG AGG TAC  
GTC CTA CGG GAA ATG CTC GCA GAG TCA TCT CGG TCG TTC CGC TCG ATG  
H D G I L I G I C T A F Y C T P I F>

09/091608

WO 97/23613

PCT/GB96/03209

26/40

1930	1940	1950	1960	
GAC GCC CTT CAC ATG CAG CCC CTG CCC CCT CCC AGG AGT AAG AGG AGC CTG CGG GAA GTG TAC GTC CGG GAC GGG GGA GGG TCC TCA TTC TCC TCG D A L H M Q A L P P R R S K R S>				
1970	1980	1990	2000	2010
AGG CTC CTG CAC AGT GAC TAC ATG AAC ATG ACT CCC CGC CGC CCC GGG TCC GAG GAC GTG TCA CTG ATG TAC TTG TAC TGA GGG GCG GCG GGG CCC R L L H S D Y M N M T P R R P G>				
2020	2030	2040	2050	2060
CCC ACC CCC AAG CAT TAC CAG CCC TAT GGC CGA CGA CGG GAC TTC GCA GGG TGG CGG TTC GTA ATG GTC GGG ATA CGG CGT CGT CGG CTG AAG CGT P T R K H Y Q P Y A P ? R D F A>				
2070				
GCC TAT CCC TCC TGA CGG ATA CGG AGG ACT A Y R S *				

FIG. 8 (contd.)

27/40

## FIG. 9

SEQUENCE OF hCTM01 / h<sub>1</sub> CD26 RECOMBINANT CHIMERIC RECEPTOR

10	20	30	40	
ATG TCT GTC CCC ACC CAA GTC CTC GGA CTC CTG CTG CTG TGG CTT ACA				
TAC AGA CAG GGG TGG GTT CAG GAG CCT GAG GAC GAC GAC ACC GAA TGT				
M S V P T Q V I G L L L L W L T>				
50	60	70	80	90
GAT GCC AGA TCC GAT ATC CAG ATG ACT CAG AGT CCA AGT ACT CTC AGT				
CTA CGG TCT ACG CTA TAG CTC TAC TGA GTC TCA GGT TCA TGA GAG TCA				
D A R C D I Q M T I C P S T I S>				
100	110	120	130	140
GCC AGT GTA GGT GAT AGG GTC ACC ATC ACT TGT AGG AGT AGT AAA AGT				
CGG TCA CAT CCA CTA TCC CAG TGG TAG TGA ACA TCC TCA TCA TTT TCA				
A S V G D R V T I T C R S S K S>				
150	160	170	180	190
CTC CTC CAT AGT AAC GGT GAC ACC TTC CTC TAT TGG TTC CAG CAG AAA				
GAG GAG GTA TCA TTG CCA CTG TGG AAG GAG ATA ACC AAG GTC GTC TTT				
L L H S N G D T F L Y W F Q Q K>				
200	210	220	230	240
CCA GGT AAA GCC CCA AAG CTC CTC ATG TAT AGG ATG AGT AAC CTC GGC				
GCT CCA TTT CGG GGT TTC GAG GAG TAC ATA TCC TAC TCA TTG GAG CGG				
P G K A P K I L M Y R M C N L A>				
250	260	270	280	
AGT GGT GTA CCA TCT AGA TTC AGT GGT AGT GGT AGT GGT ACT GAG TTC				
TCA CCA CAT GGT AGA TCT AAG TCA CCA TCA CCA TCA CCA TGA CTC AAG				
S G V P S R F S G S G S G T E F>				
290	300	310	320	330
ACT CTC ACT ATC AGT AGT CTC CAG CCA GAT GAT TTC GGC ACT TAT TAT				
TGA GAG TGA TAG TCA TCA GAG GTC GGT CTA CTA AAG CGG TGA ATA ATA				
T L T I S S I Q P D D F A T Y Y>				
340	350	360	370	380
TGT ATG CAG CAT CTC GAA TAT CCA TTC ACT TTC GGT CAG GGT ACT AAA				
ACA TAC CTC GTC GAA GAG TTT ATA GGT AAG TGA AAG CCA GTC CCA TCA TTT				
C M Q H I E Y F I F G I C T K>				
390	400	410	420	430
CTA GAA GTC AAA CCT ACG CCT GGT CCG CCA CGG TCA GGT CCG CGG TCA				
CAT CTT CAT TTT CCA TCC CCA CGG CCT CGG ACT CCA CGG CCT CGG ACT				
V E V K R T S S G S I G T S G S>				

09/091608

WO 97/23613

PCT/GB96/03209

28/40  
FIG. 9 (contd.)

440                    450                    460                    470                    480  
 CGT GGC GGA GGG TCA GGT GGC GGA GGG TCA GGT GGC GGA GGG TCA CAG  
 CCA CGG CCT CCC AGT CCA CGG CCT CCC AGT CCA CGG CCT CCC AGT GTC  
 G G G G S G G G S G G S G G S Q>

490                    500                    510                    520  
 ATT CAG CTG GTG CAG TCT GGA GCA GAG GTG AAG AAG CCT GGA TCT TCT  
 TAA GTC GAC CAC CTC AGA CCT CGT CTC CAC TTC TTC GGA CCT AGA AGA  
 I Q L V Q S G A E V K K P G S S>

530                    540                    550                    560                    570  
 GTG AAG GTG TCT TCT AAG GCA TCT GGA TAC ACC TTC ACC GAC TAC TAC  
 CAC TTC CAC AGA AGA TTC CCT AGA CCT ATG TGG AAG TGG CTG ATG ATG  
 V K V S D K A S G Y T F T S D Y Y>

580                    590                    600                    610                    620  
 ATT AAT TGG ATG AGA CAG GCA CCT GGA CAG GGA CTC GAG TGG ATT GGA  
 TAA TTA ACC TAC TCT GTC CGT GGA CCT GTC CCT GAG CTC ACC TAA CCT  
 I N W M R Q A P G Q G L E W I G>

630                    640                    650                    660                    670  
 TGG ATT GAC CCT GGA TCT GGA AAT AGA AAG TAC AAT GAG AAG TTC AAG  
 ACC TAA CTG GGA CCT AGA CCT TTA TGT TTC ATG TTA CTC TTC AAG TTC  
 W I D P G S G N T K Y N E K F K>

680                    690                    700                    710                    720  
 GGA AGA GCA ACA CTG ACA GTG GAC ACA TCC ACC AAT ACC CCC TAC ATG  
 CCT TCT CCT TGT GAC TCT CAC CTG TCT AGG TCC TTA TGG CGG ATG TAC  
 G R A T L T V D T S T N T A T M>

730                    740                    750                    760  
 GAG CTG TCT TCT CTG AGA TCT GAG GAC AGA GCA TTC TAC TTC TGT GCA  
 CTC GAC AGA AGA GAC TCT AGA CTC CTG TGT CCT AAG ATG AAG AGA CCT  
 E L S S L R S E D T A F Y F C A>

770                    780                    790                    800                    810  
 AGA GAG AAG ACC ACC TAC TAC TAC GCA ATG GAC TAC TGG GGA CAG CGA  
 TCT CTC TTC TGG TGG ATG ATG ATG CCT TAC CTG ATG ACC CCT GTC CCT  
 R E K T T Y Y A M D Y W G I G>

820                    830                    840                    850                    860  
 ACA CTG CTG AGA CTG TCT TCT GCA TCA ACC AAG CGG CGG ACT ACT GAC  
 TGT GAC CAC TCT CTC AGA AGA CGG AGT TGG TTC CGG CGG TCA TCA CTC  
 T L V T V S S A S T K G P T S D>

870                    880                    890                    900                    910  
 AAA ACT GAC AGA TGG CCA CGG TGG CGA AAA CGG AAA GAC CTT TGT CGA  
 TTT TCA CTG TCT AGC CGT CGG AGG CGT TTT CGG TTT CGG CGA AGA CCT  
 K T H T C P P S P K S Y H L J P>

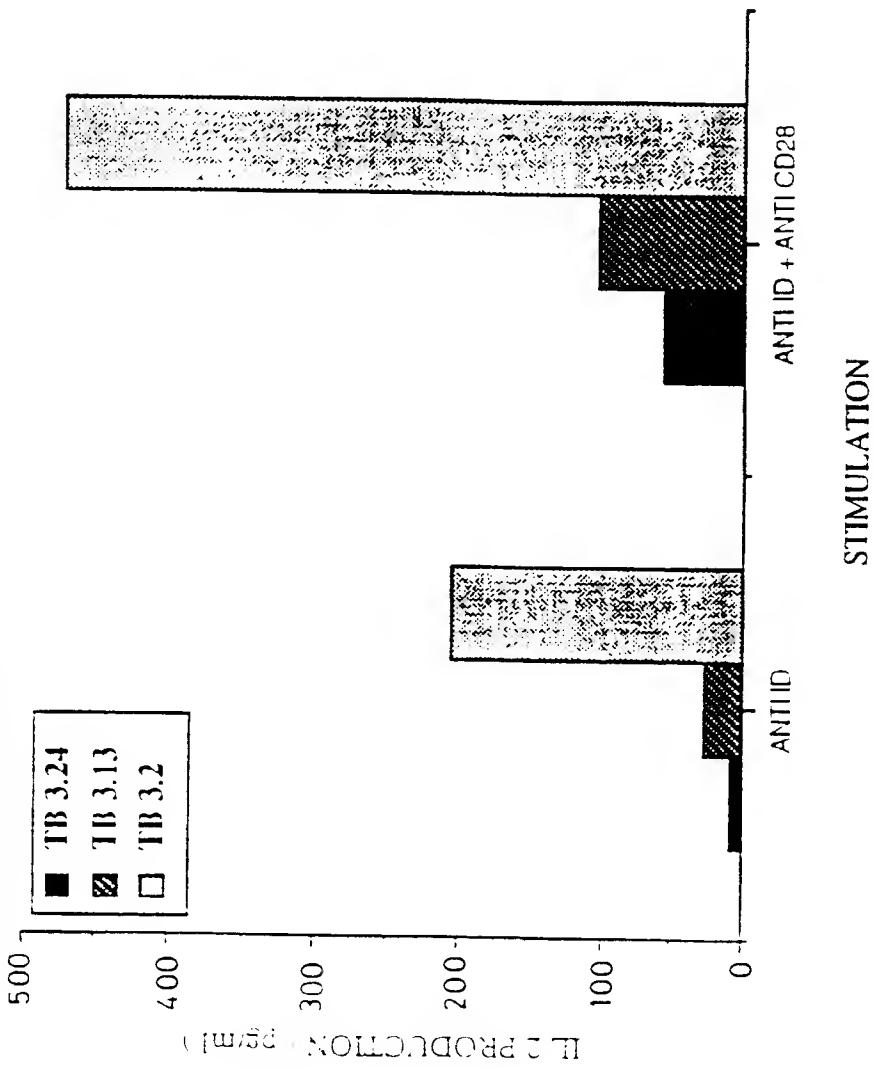
29/40

920	930	940	950	960
AGT CCC CTA TTT CCC GGA CCT TCT AAG CCC TTT TGG GTG CTG GTG GTG				
TCA GGG GAT AAA GGG CCT GGA AGA TTC GGG AAA ACC CAC GAC CAC CAC				
S P L F P G P S K P F W V L V V >				
970	980	990	1000	
GTT GGT CGA GTC CTG CCT TGC TAT AGC TTG CTA GTA ACA GTG GCC TTT				
CAA CCA CCT CGG GAC CGA AGG ATA TCG AAC GAT CTT TGT CAC CGG AAA				
V G G V L A C Y S L L V T V A F >				
1010	1020	1030	1040	1050
ATT ATT TGC TGG GTG AGG AGT AAG AGG AGG AGG CTC CTG CAC AGT GAC				
TAA TAA AAG AGG GAC CGC TCG TCA TTC TCG TCG TCG GAG GAC GTG TCA CTG				
I I F W V F S K R S R L I H C D >				
1060	1070	1080	1090	1100
TAC ATG AAC ATG ACT CCC CGC CCC CCC GGG CCC ACC CCC AAG GAT TAC				
ATG TAC TTG TAC TGA GGG GCG GCG GGG CCC GGG TGG GCG TTC GTA ATG				
Y M N M T P R R P G P T R K H Y >				
1110	1120	1130	1140	
CAG CCC TAT CCC CCA CGA CGC GAC TTC GCA GCG TAT CGC TCC TGA				
GTC GGG ATA CGG GGT GGT GCG CTG AAG CGT CGG ATA CGG AGG ACT				
Q P Y A P P R D F A A Y R S *				

FIG. 9 (contd.)

30/40

FIG. 10  
CO-STIMULATION OF CELL LINES EXPRESSING A TCR ZETA CHIMERIC RECEPTOR  
WITH ANTI CD28 ANTIBODY



09/091608

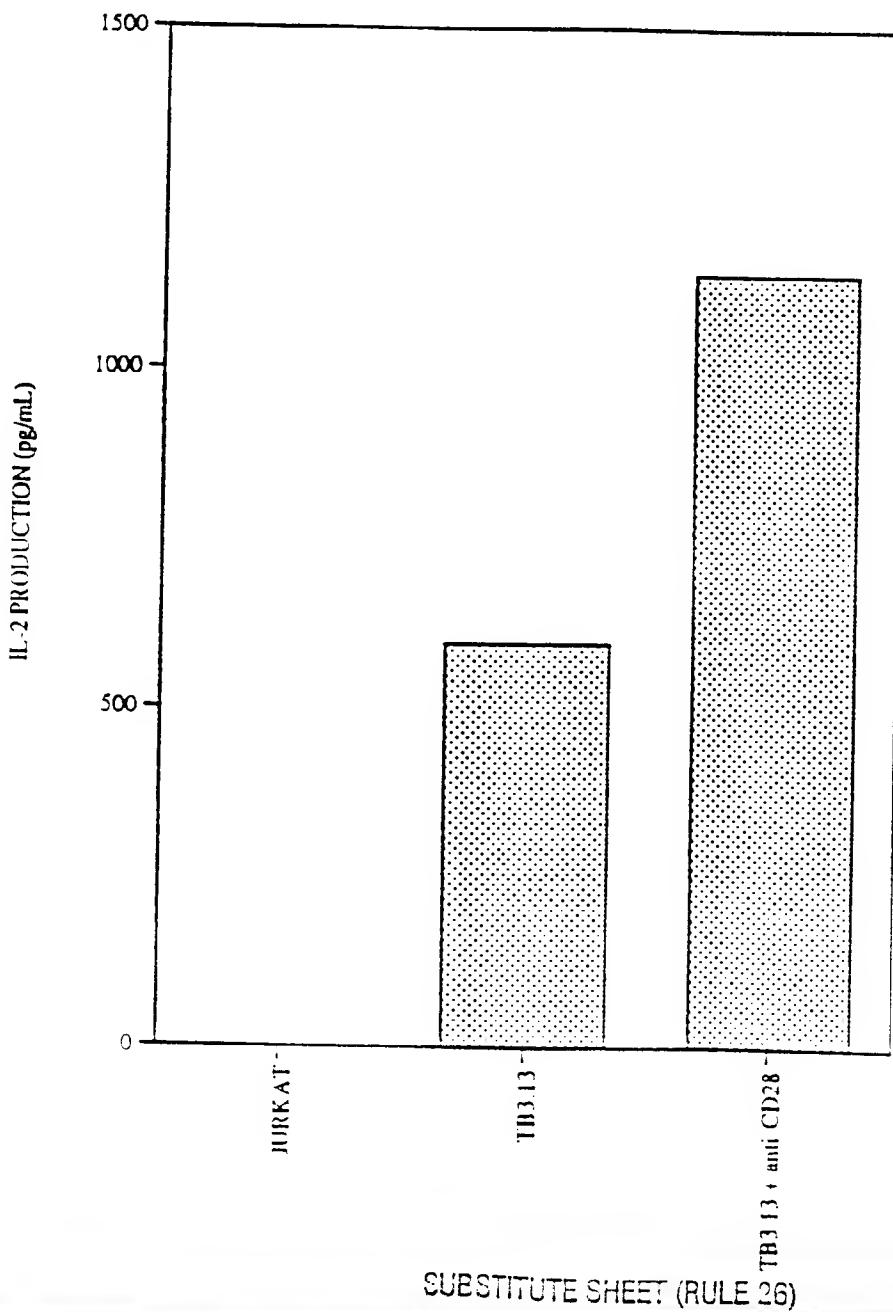
WO 97/23613

PCT/GB96/03209

31/40

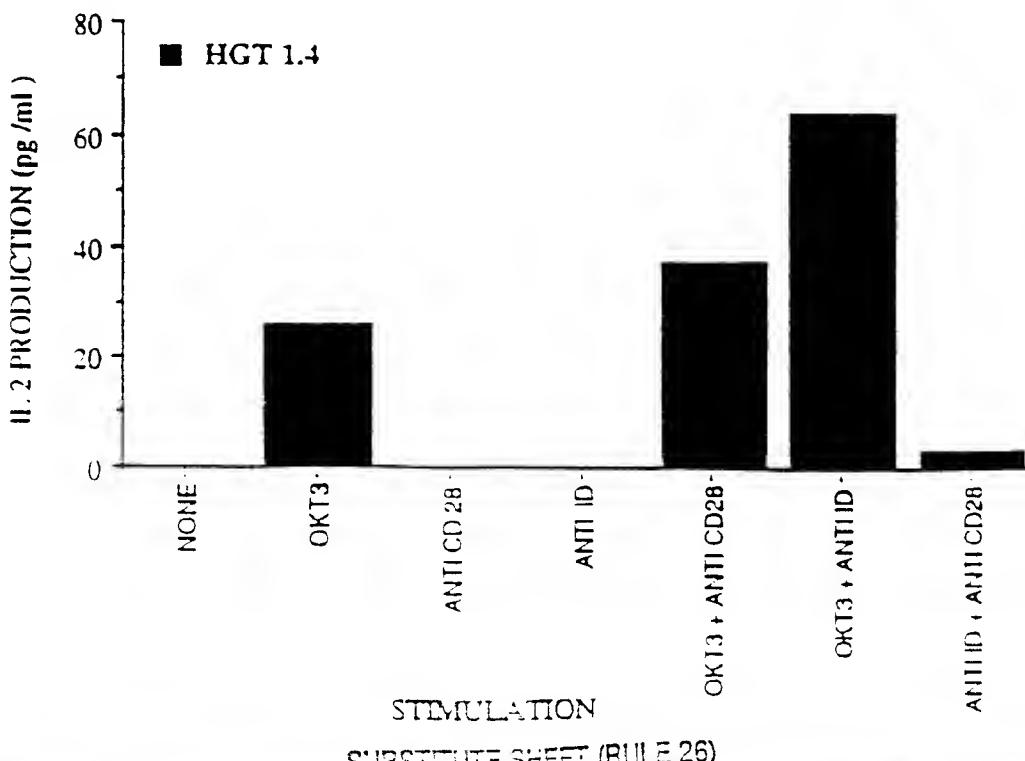
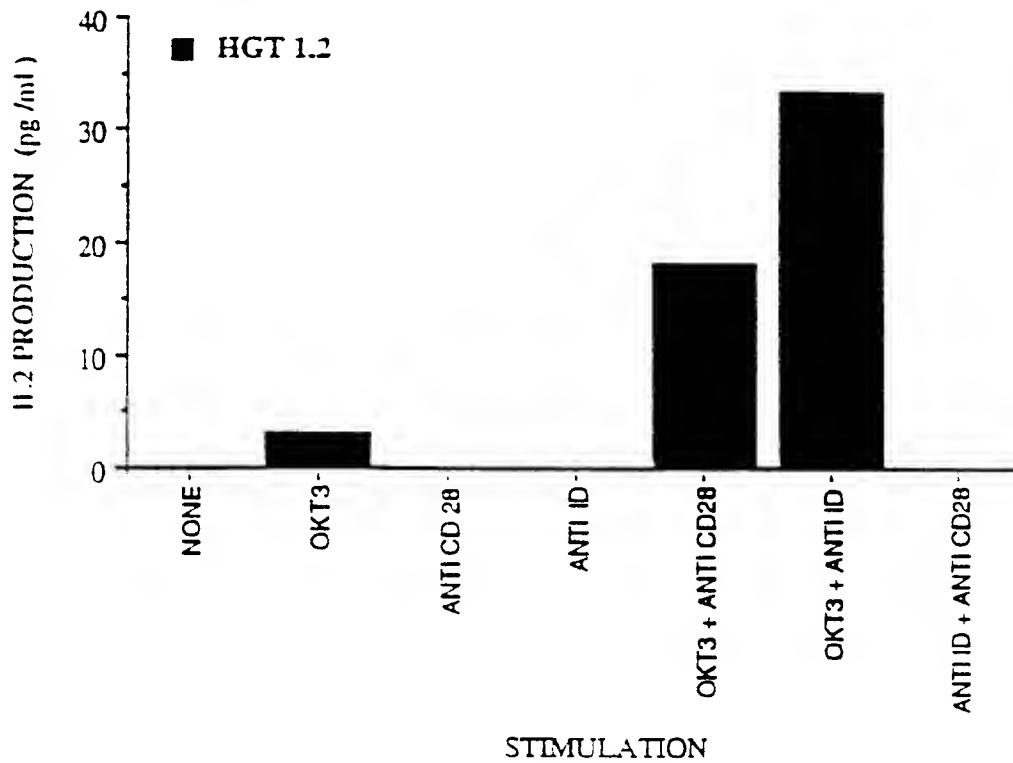
FIG.11

STIMULATION WITH ANTIGEN POSITIVE CELLS.MCF-7



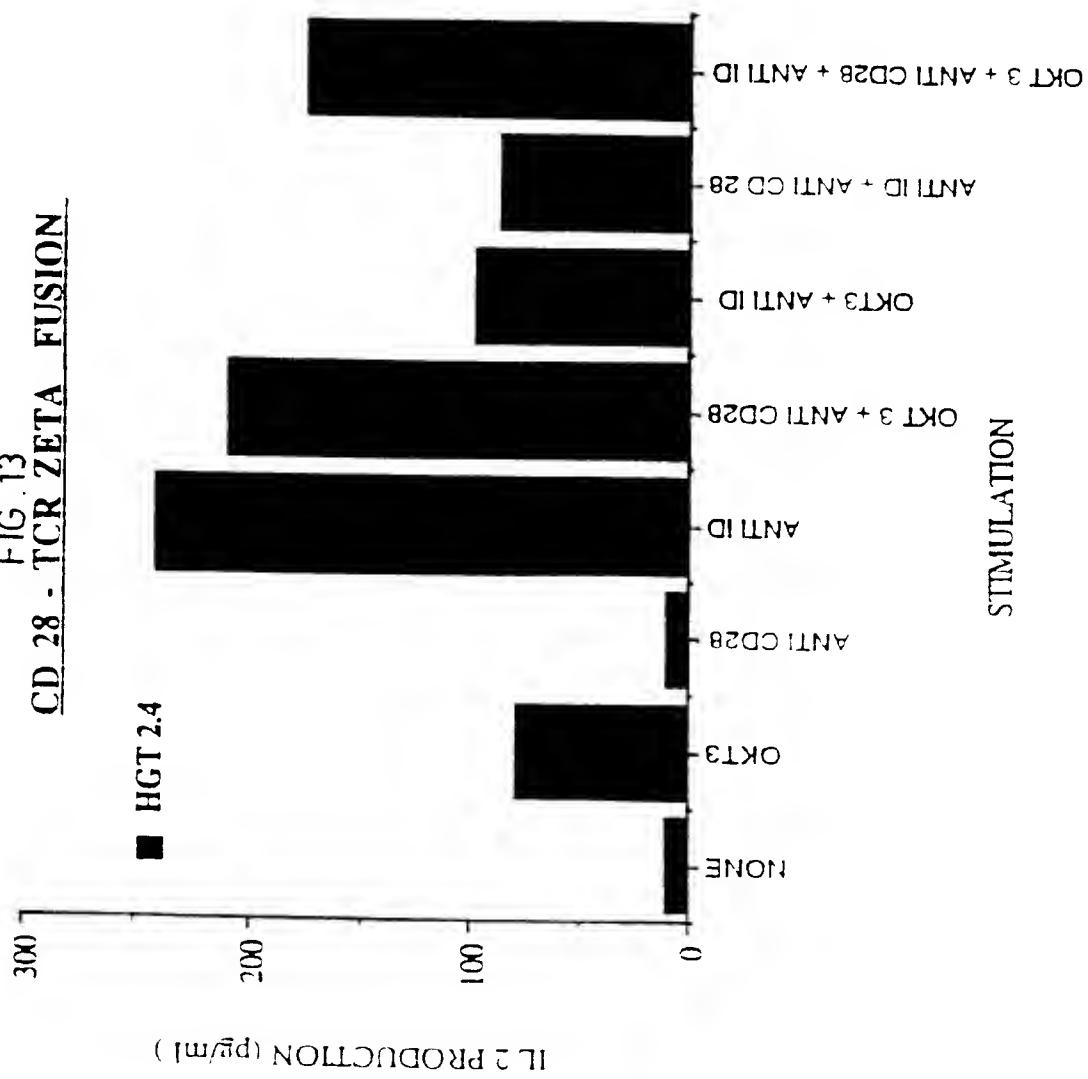
32/40

FIG. 12

IL2 PRODUCTION IN RESPONSE TO VARIOUS STIMULI

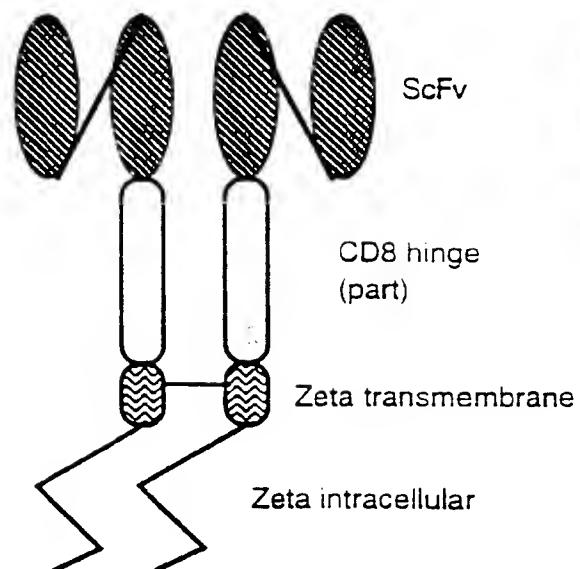
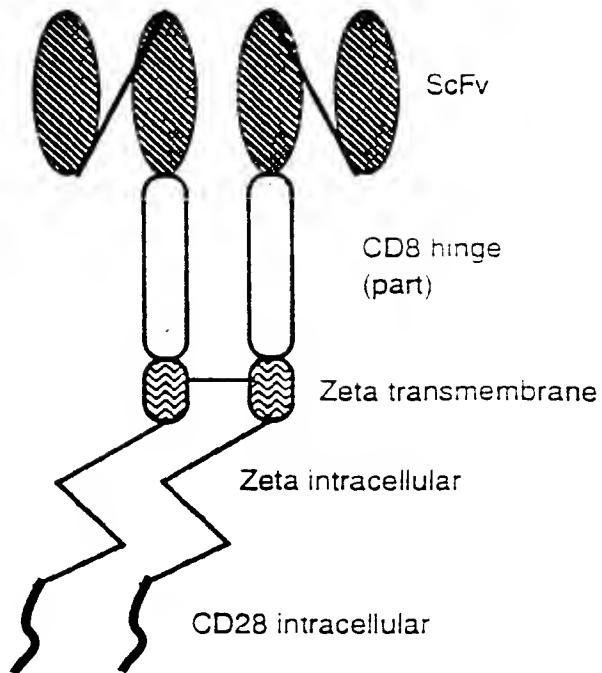
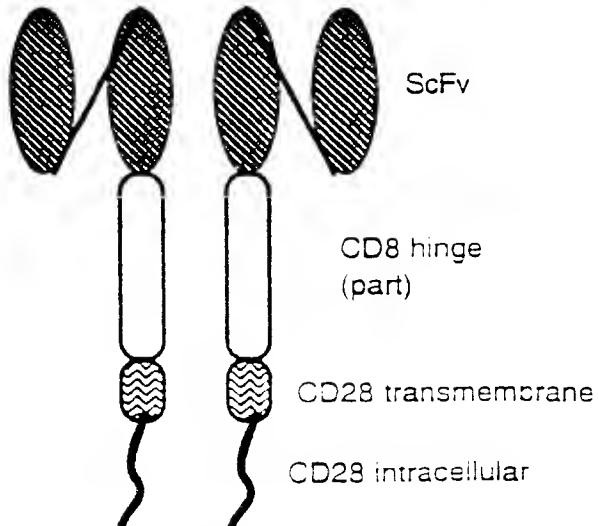
33/40

CD 28 - TCR ZETA FUSION



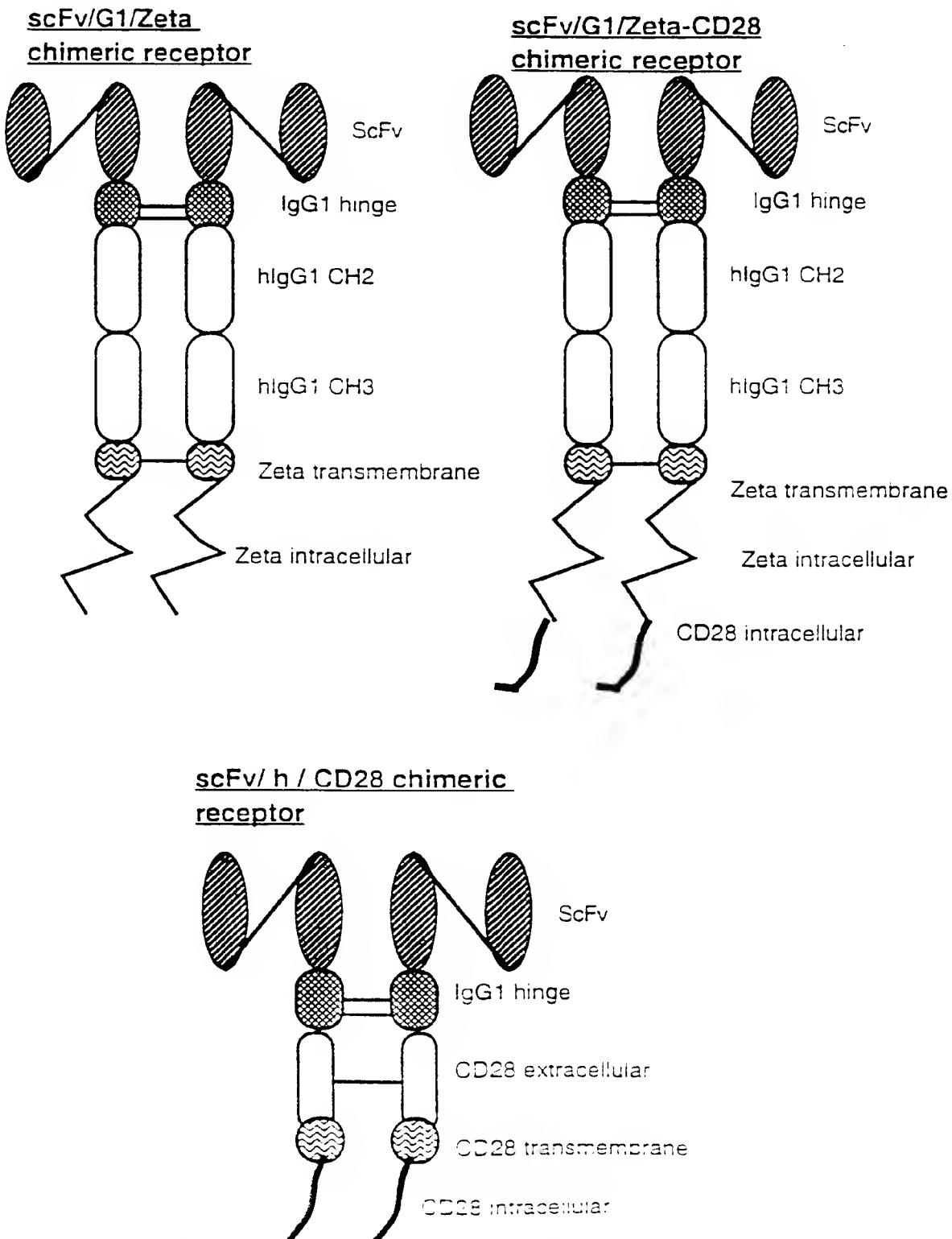
34/40

FIG. 14

scFv / CD8 / Zeta  
chimeric receptorscFv / CD8 / Zeta-CD28  
chimeric receptorscFv / CD8 / CD28  
chimeric receptor

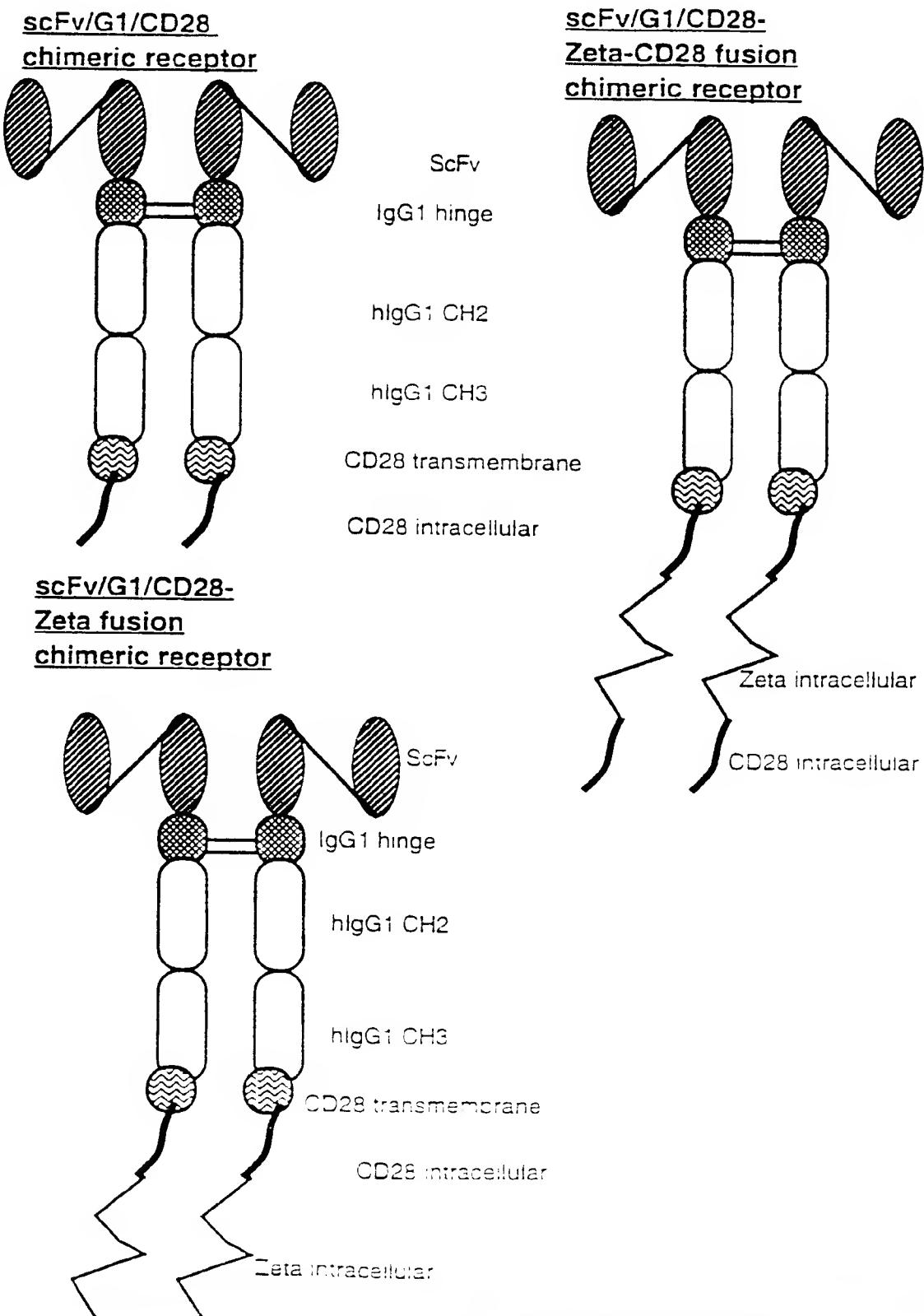
35/40

FIG. 15



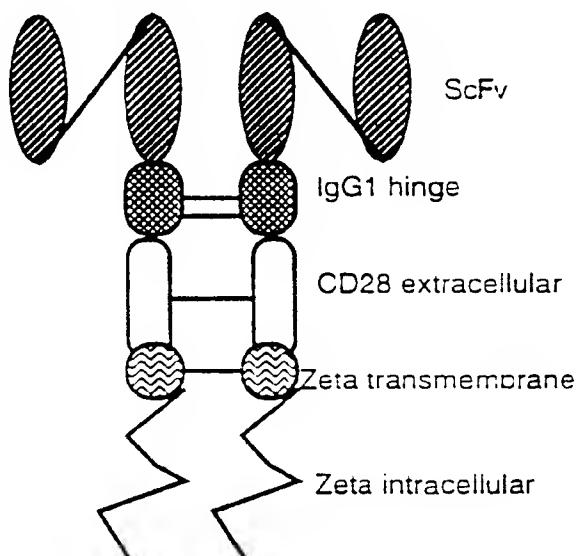
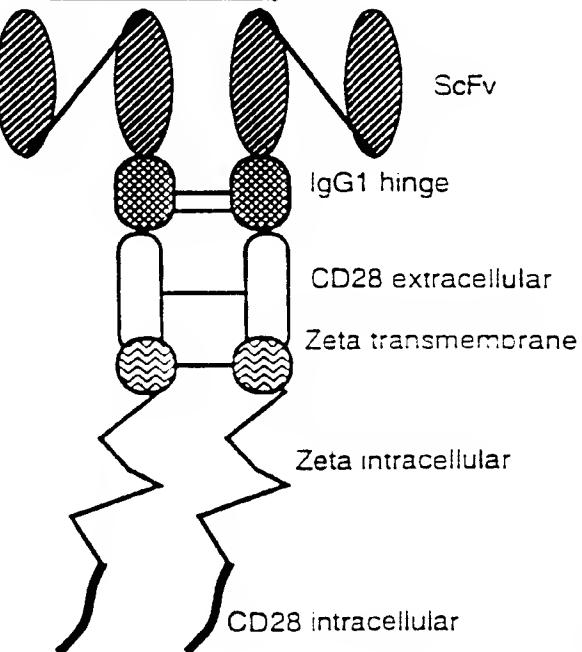
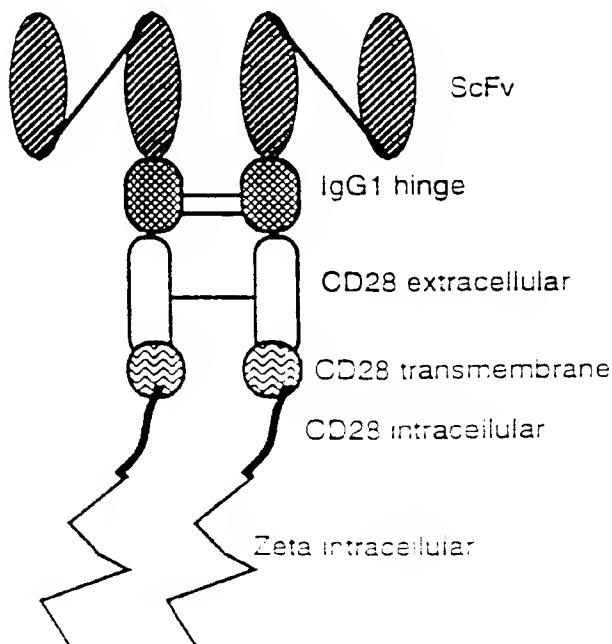
36/40

FIG. 16



37/40

FIG. 17

scFv/h.28/Zeta  
chimeric receptorscFv/h.28/Zeta-  
CD28 fusion  
chimeric receptorscFv/h.28/CD28-  
Zeta fusion  
chimeric receptor

38/40

FIG. 18  
Surface expression of CD28-chimeras  
in transfected Jurkat cell lines determined  
by FITC-CD33 staining

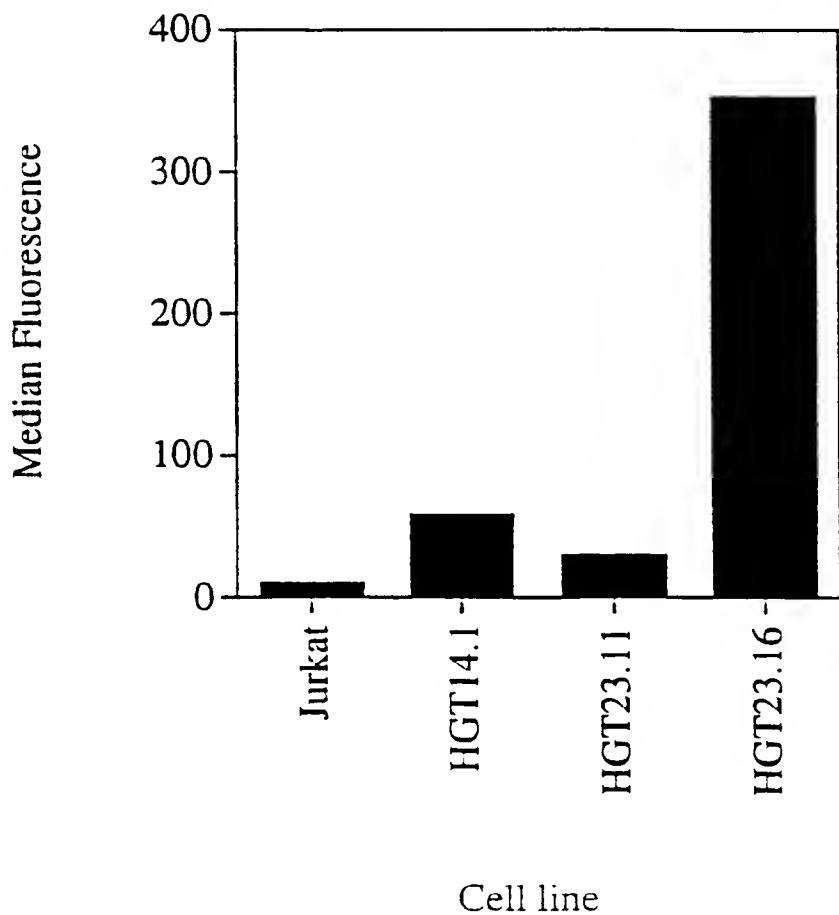
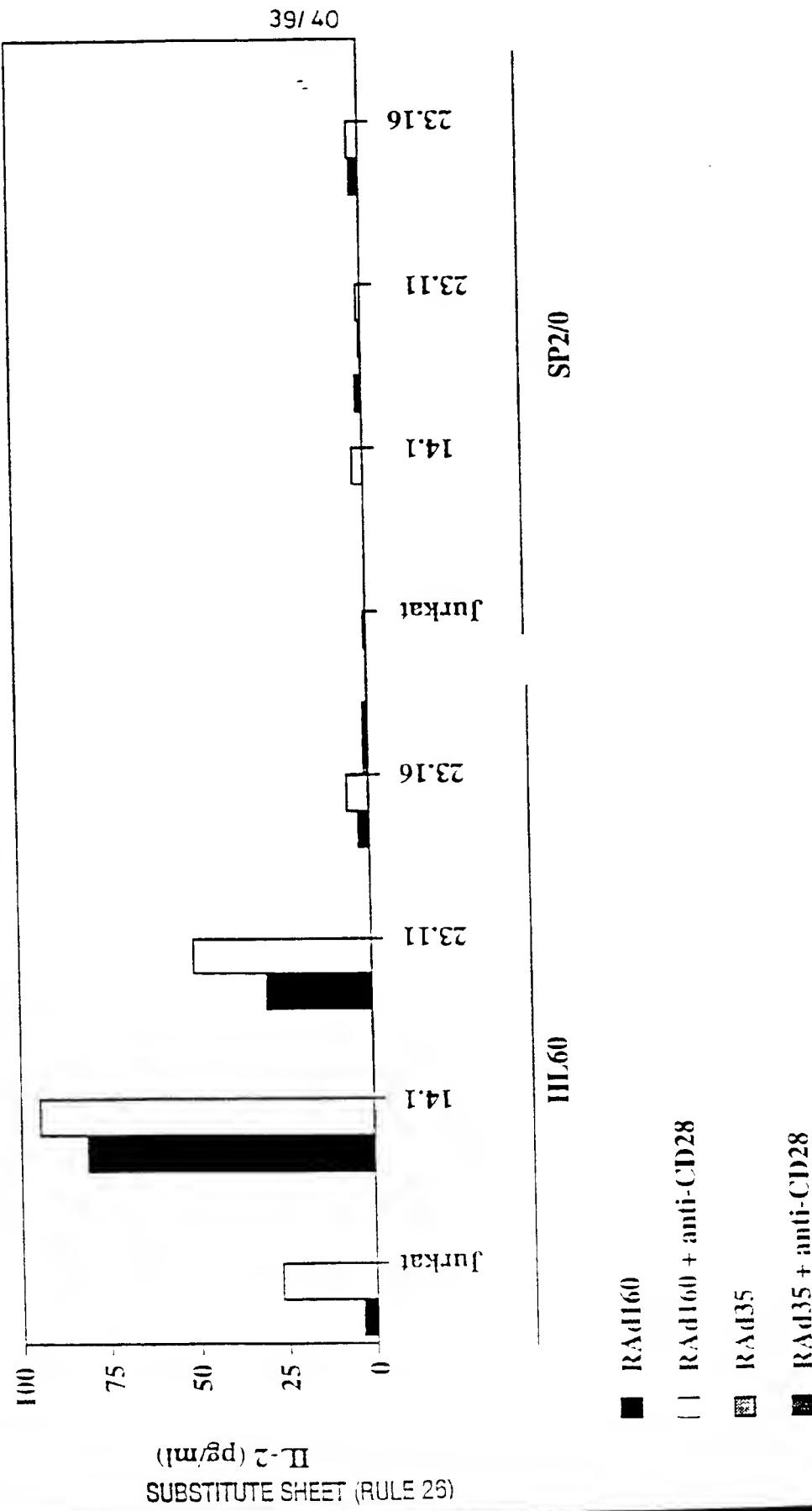


FIG. 19  
IL-2 production by Jurkat cell lines expressing  
p67-CD28 chimeras on infection with RAd160  
stimulated with target cells



09/09/08

WO 97/23613

PCT/GB96/03209

FIG. 20

**51Cr Release Assay**  
**Adenovirus infected CD8+ve peripheral**  
**blood lymphocytes with HL60 target cells**

